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CONTENTS AND SUBJECT INDEX

Present Day Proctology: Chairman's Address. E. H. Terrell, M.D., Richmond, Va. 529

Chronic Glomerulonephritis and the Nephrotic Syndrome: A Follow-Up Investigation of Patients Treated with Acacia. Raymond E. Smalley, M.D., and Melvin W. Binger, M.D., Rochester, Minn. 532

Septicemia and Bacterial Endocarditis Resulting from Heroin Addiction. Hugh Hudson Hussey, M.D.; Thomas F. Keliher, M.D.; Bertram F. Schaefer, M.D., and B. J. Walsh, M.D., Washington, D. C.....535

The Treatment of Early and Latent Syphilis in Nine to Twelve Weeks with Triweekly Injections of Mapharsen. Harry Eagle, M.D., Baltimore 538

Intensive Arsenotherapy. A. Benson Cannon, M.D.; Jerome K. Fisher, M.D.; Juan J. Rodriguez, M.D.; Guila F. Beattie, M.D., and Eugenia Maechling, Ph.D., New York..544

Combined Fever and Arsenotherapy in the Intensive Treatment of Early Syphilis. Evan W. Thomas, M.D., and Gertrude Wexler, M.D., New York 550

Papers of Dr. Eagle, Drs. Cannon, Fisher, Rodriguez, Beattie and Maechling and Drs. Thomas and Wexler discussed by Drs. Rattner, Strakosch, Curtis, Schwemlein, Driver, Kile, Schoch, Eagle, Fisher and Thomas.

Massive Arsenotherapy for Syphilis. Cooperating Clinics of New York and Midwestern Groups.....554

The Initial Neurologic and Psychiatric Syndrome of Pulmonary Growth. Major Dr. A. M. Meerloo, Royal Netherland Army.....558

CLINICAL NOTES

Myelopathy as a Result of Intensive Treatment of Syphilis with Mapharsen. A. L. Sahs, M.D., and Ruben Nomland, M.D., Iowa City 560

COUNCIL ON PHARMACY AND CHEMISTRY

Pathogenic Bacteria, Rickettsias and Viruses as Shown by the Electron Microscope: I. Morphology. Stuart Mudd, M.D., and T. F. Anderson, Ph.D., Philadelphia 561

New and Nonofficial Remedies..571

EDITORIALS

Punishment for Venereal Disease in the Armed Forces Ended by Congress 572

Chronic Gastritis 572

Toxicity of Rancid Lard.....573

CURRENT COMMENT

Chicago Venereal Disease Control Program 574

The Relationship of Fluorescent Porphyrins to Cancer.....574

Motivations for Treason.....574

(Subject Index on next page)

MEDICINE AND THE WAR

The Army 575

ORGANIZATION SECTION 577

★ ★ ★

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See also SAUNDERS Announcement on Pages 3, 4, 5

A. M. A. panel discussion on treating early syphilis *538-552
Abdomen, gauze sponge cause adhesions?....603
surgery, early rising after....ab-593
Abortion, Rh factor role in....ab-601
Acacia in glomerulonephritis and nephrotic syndrome *532
Acid, ascorbic, working in hot climates..ab-591
nicotinic, fluorescent factor F_2....ab-594
Adhesions, gauze sponge cause?....603
Air Raids, patients *not* up day after labor.C-588
Ambulance given to Army medical dept.....375
Androgens, excretion in homosexuality....603
Anesthesia, continuous caudal, in thrombophlebitis ab-591
Arsphenamine in syphilis....*544; *554
Arteries, coronary occlusion, differentiating ab-590
Asthma, breathing therapy....ab-593
Bacteria, electron micrograph....*561
Belgians, grateful for liberation....583
Beta vulgaris and pollinosis....583
Beveridge plan, doctor's view....582
Bismuth plus mapharsen in syphilis....*538
Bladder paralysis from mapharsen....*560
Blood bilirubin in jaundice diagnosis....ab-601
calcium level in psoriasis....603
groups, jaundice from serum....ab-595
phosphatemia in jaundice diagnosis....ab-601
sedimentation rate, raised, in lung tumors *558
sulfonamide concentrations....ab-590
Board Examinations....589
Book Notices....602
Books Received....Adv. Page 48
Breast cancer and fluorescent porphyrins.E-574
Bronchiectasis, lobectomy for....ab-600
Bureau of Investigation....587
Bureau of Legal Medicine and Legislation...589
Burns, fibrinogen and thrombin for....ab-596
Cancer, estrogens induce?....604
fluorescent porphyrins relation to....E-574
Chicago venereal disease control program.E-574
Chinese, research at Oxford and Cambridge 582
Chiropractic Practice Acts: licenses; revocation MI-589
Convalescence, early rising after abdominal section ab-593
patients *not* up day after labor....C-588
Cornea vascularization: ariboflavinosis....ab-595
Correspondence....588
Council on Pharmacy and Chemistry....561
Dalton, John, centenary....582
Dawson, Lord, on national health service..582
Deaths....584
Dermatitis from arsphenamine....*548
Dusting Powder for surgical gloves....C-588
Editorials....572
Electric treatment (nonconvulsive) in depression ab-601
Electron microscope....*561
Emphysema from ingesting kerosene....ab-597
Encephalitis, toxic, from arsenotherapy *541; *547; *550; *557
Endocarditis, acute bacterial, from heroin addiction *535
Endocrine imbalance and homosexuality..603
Erythroblastosis, fetal, and Rh factor....ab-601
Estrogens, excretion in homosexuality....603
overuse induce cancer?....604
Eye fatigue symptoms and riboflavin....ab-595
F_2 fluorescent factor in urine....ab-594
Fever, therapeutic, plus mapharsen....*550
Fibrinogen coagulum to remove renal calculi ab-596
treatment of burns....ab-596
Fistula, arteriovenous....ab-594
Fluorescent factor F_2 in urine....ab-594
porphyrins, relation to cancer....E-574
Foreign Letters....582
"Gas pains"....604
Gauze sponge cause abdominal adhesions?...603
Glomerulonephritis, chronic, acacia for....*532
Glycosuria in meningitis....ab-592
Goiter, toxic, thiouracil for....ab-596
Gonorrhea, penicillin for....575; ab-595; ab-599
Granuloma, talcum powder....C-588
Hanger test in jaundice....ab-601
Harris drip proctoclysis, postoperative use...604
Heart electrocardiogram in coronary occlusion and pericarditis....ab-590
great left electrical axis deviation....ab-590
Heat, working in, and vitamin C....ab-591
Hemangioma, cavernous, of lung....ab-594
Heroin addiction, septicemia and endocarditis from *535
Homosexuality and endocrine imbalance....603
Hospital, Rodriguez General....576
Hyperthyroidism, thiouracil for ab-596
Industrial exposure to calomel....604
working in heat and vitamin C....ab-591
Infanis, mortality of breast and bottle fed..603
Influenza outbreak in 1943....ab-600
Insecticide: PDB....575
Jaundice from serum....ab-595
diagnosis (differential)....ab-601
toxic, from arsenotherapy....*541
Kerosene, pneumonia, pneumothorax and emphysema from ingesting....ab-597
Kidneys, calculi, fibrinogen coagulum to remove ab-596
nephrotic syndrome, acacia for....*532
Lard, rancid, toxicity....E-573
Leg paralysis after mapharsen treatment..*560
Leukemia, monocytic, sore mouth in....ab-597
Leukopenia after arsphenamine....*548
Liver inflammation from arsphenamine....*548
Lung, agenesis....ab-598
apical opacities....603
cavernous hemangioma....ab-594
lobectomy for bronchiectasis....ab-600
tumors, neurologic syndrome....*558
Malaria and quinine, Argentina....583
control in Pacific....575
Mapharsen, toxicity....*538; *550; *560
use in syphilis....*554
Marriages....583
Medical Economic Abstracts....577
Medical Examinations and Licensure....589
Medical Service plans, progress....OS-577
Medicine and the War....575
Medicolegal Abstracts....589
Meerloo, A. M., motivations for treason.E-574
Meetings, Coming Meetings....577
Meningitis, glycosuria in....ab-592
penicillin for....ab-599
sulfadiazine for....ab-593
tuberculous ab-600
Mental Depression, electric therapy....ab-601
sign of lung tumor....*558
Mercurous chloride, industrial exposure....604
Methylene blue peritoneal tap test....ab-594
Microscope, electron, examination of bacteria, rickettsias and viruses....*561
Mononucleosis, infectious, heterophile antibody reaction in....ab-593
Morphine, *di*acetyl (heroin) addiction....*535
Moth, urticaria from....ab-598
Mountbatten praises 20th General Hospital..575
Mouth, "sore," in monocytic leukemia..ab-597
Myasthenia gravis, thymectomy for....ab-598
Negroes, syphilis in....*538; ab-592
Neoarsphenamine in syphilis....*554
Nephritis, glomerular, acacia for....*532
Neuralgia in lung tumor....*558
New and Nonofficial Remedies....571
News....578
Organization Section....577
PDB, new deodorant....575
Paralysis after mapharsen therapy....*560
in pulmonary tumor....*558
Patients *not* up day after labor....C-588
Pediatrics, chair of child health, London....582
Pellagra in hospital patients....ab-594
Penicillin treatment of gonorrhea....575; ab-595; ab-599
treatment of meningitis....ab-599
Peptic Ulcer, perforated, methylene blue peritoneal tap test....ab-594
Pericarditis, postoperative....ab-590
Peritoneal tap using methylene blue....ab-594
Phthalylsulfathiazole, clinical use....ab-597
Physicians, Belgian, status during German occupation 583
Pickhardt, W. L., German war prisoner..575
Plaster, closed method prevents shock..ab-595
Pneumonia, atypical primary, apical opacities 603
from ingesting kerosene....ab-597
Pneumothorax, from ingesting kerosene...ab-597
Pollinosis and Beta vulgaris....583
Porphyrins, fluorescent, as carcinogens....E-574
Pregnancy, Rh factor....ab-601
Proctoclysis, Harris drip, postoperative use..604
Proctology, present day....*529
Pseudomonas septicemia from heroin addiction *535
Psoriasis, treatment....603
Psychiatry syndrome of pulmonary growth.*558
Psychology, motivations for treason....E-574
Puerperium, patients *not* up on 1st day....C-588
Queries and Minor Notes....603
Quinine supply and malaria, Argentina....583
Rectum, diseases *529
Harris drip proctoclysis 604
Rehabilitation, vocational OS-577
Respiration, therapeutic, in asthma....ab-593
Rh Factor and jaundice from serum....ab-595
in obstetrics ab-601
Riboflavin deficiency and corneal vascularization ab-595
Rickets in Bristol children....ab-600
Rickettsias, electron micrographs....*561
Rubber Gloves, dusting powder for....C-588
Septicemia from heroin addiction....*535
Shock, closed plaster method prevents....ab-595
Silicates cause silicosis?....C-588
Skin graft, surgical use....ab-599
Society Proceedings....577
Spinal Cord lesion from mapharsen....*560
Sponge, gauze, cause adhesions?....603
Staphylococcus aureus, septicemia from heroin addiction *535
State Board Examinations....589
Stomach, cancer and chronic gastritis....E-572
Sulfadiazine in meningitis....ab-593
Sulfanilamide in tuberculosis....ab-592
Sulfapyridine in tuberculosis....ab-592
Sulfonamide concentrations in blood....ab-590
resistant acute gonorrhea, penicillin for ab-595; ab-599
treatment of gonorrhea....575
Surgery, cutis graft transplant in....ab-599
early rising after....ab-593
"gas pains" 604
Harris drip proctoclysis 604
Syphilis, A. M. A. panel discussion on intensive treatment....*538-552
arsphenamine by syringe method for; 7 plans *544
fever plus mapharsen 10-day treatment..*550
in Negroes with tuberculosis....ab-592
mapharsen for, also with bismuth....*538
mapharsen for, myelopathy results....*560
neoarsphenamine, arsphenamine, typhoid vaccine or mapharsen for: 6 methods..*554
Talcum powder granulomas....C-588
Tetanus, inject antiserum via cisterna....ab-591
Thiouracil for thyrotoxic patients....ab-596
Thrombin surface treatment of burns....ab-596
Thrombophlebitis, continuous caudal anesthesia in ab-591
Thymectomy in myasthenia gravis....ab-598
Tonics and Sedatives....Adv. Page 36
Treason, motivations for: Meerloo's lecture.E-574
Tuberculosis, apical opacities....603
nutrition in ab-592
pulmonary, with syphilis in Negro....ab-592
sulfanilamide and sulfapyridine in....ab-592
Typhoid vaccine induced fever in syphilis *550; *554
Ultraviolet rays for psoriasis....603
Urine, fluorescent factor F_2 in....ab-594
Urticaria from brown moth....ab-598
Venereal Disease, end punishment for in armed forces E-572
control program, Chicago....E-574
Virus, comparative sizes....*568
electron microscopic study....*561
Vitamin B complex, pellagra in hospital patient receiving....ab-594
C and working in hot climate....ab-591
D treatment of psoriasis....603
deficiency, toxicity of rancid lard....E-573
Vocational rehabilitation program....OS-577
Washington Letter....577
Whooping Cough, lyophile human serum..ab-598
World War II, ambulance given Army Medical Dept. 575
Belgians' gratitude 583
gonorrhea treatment 575
heroes: Benson (O. O., Jr.)....576
heroes: Doherty (E. J.)....576
heroes: Feves (L. J.)....576
heroes: Frese (F. J.)....576
heroes: Jensen (W. S.)....576
heroes: Johnson (H. M.)....576
heroes: Lage (G. H.)....576
heroes: Makart (C. D.)....576
heroes: Persing (A. V., Jr.)....576
heroes: Thorpe (G. L.)....576
hospital unit, 20th General, praised....575
hospitals, Rodriguez General....576
London blitz and childbirth....C-588
malaria control in Pacific....575
motivations for treason....E-574
prisoner: Pickhardt (W. L.)....575
venereal disease punishment....E-572
Yellow Fever, jaundice after....ab-595

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PRESENT DAY PROCTOLOGY

CHAIRMAN'S ADDRESS

E. H. TERRELL, M.D.

RICHMOND, VA.

A cursory review of the history of medicine reveals that some interest has been manifested in proctology for many centuries. The etiology and pathology of the many diseases affecting the lower part of the bowel were not understood, and treatment was of the crudest and most unscientific sort until toward the end of the last century. It was not until about this time that any serious and orderly consideration of them was undertaken. Considerable impetus was given these studies by Dr. Joseph Mathews of Louisville, Ky., who has been considered the father of proctology. He was the first physician in the world to limit his practice to this field. Since his time there has been a continued and progressive advancement in the knowledge of these diseases.

Not unlike some other specialties, proctology has had to overcome certain prejudices, which were brought about largely because of indifference on the part of the profession or, probably to a greater extent, by incompetence. At any rate, this was for a long time a lucrative field for the advertising quack. During the latter part of the last century, and extending well into the early part of the present, the stigma of charlatanism was closely associated with proctology. There were, however, during this period a few ethical specialists who were doing good scientific work. Unlike the irregulars, they had nothing to conceal from either their fellow practitioners or their patients. For them there were no secret formulas, but whatever knowledge they possessed was given openly and freely. The more determined and enthusiastic of these in 1899 banded together in an organization which they called the American Proctologic Society, the purpose of which was the study and dissemination of knowledge pertaining to diseases of the rectum and colon. Since then great strides have been made in the understanding of the etiology of these various diseases; also greatly improved methods of diagnosis and treatment have been instituted. Now the skepticism toward proctology formerly held by the profession and some of the public has been, I believe, completely dissipated, and it holds as honorable a place as the other surgical specialties.

Read before the Section on Gastro-Enterology and Proctology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 15, 1944.

The proper limitations of the specialty have been much discussed but not determined definitely. There are some who confine their efforts to treatment of diseases within reach of the sigmoidoscope, probably 10 or 12 inches from the anus; others include surgery of the lower colon, colostomies and abdominoperineal resections for cancer or other conditions. Whether a proctologist shall attempt such a formidable operation as a resection is, of course, primarily dependent on his capabilities. If one has been well trained in this type of surgery he should by all means be encouraged to continue it, provided he has a sufficient number of these operations to maintain the proper technic. No operator wishes to shirk his duty or responsibility, but operations for cancer of the lower bowel, at best, carry with them much anxiety and oftentimes grief as well. When all has been said pro and con, each individual must be the judge of his own qualifications.

Proctology is one of the few specialties not overcrowded. There are many large and prosperous communities with no physician claiming any special knowledge in this line of work. Almost any one of these would support handsomely an energetic and well trained man. For a long time a gradually increasing interest has been shown in the study of proctology, although many wouldbe students are handicapped because there is an insufficient number of places where proper training can be obtained. While at present nearly every medical school has a department in proctology for undergraduates, the daily schedule is so crowded that the student, at best, can obtain only a rudimentary knowledge of the rectum and its diseases. There are, of course, a few postgraduate institutions with courses in proctology, but these can accommodate only a limited number of students. At present the best opportunity for a young man to receive proper training is to become associated, if possible, with an older and well established proctologist. Unfortunately, there are only a few such opportunities.

Since specialists in rectal diseases are relatively few, a large amount of this work is done by the general surgeon and much, not requiring surgery, by the general practitioner or internist. It is most gratifying to note that among our best surgeons and internists there is an increasing tendency toward more frequent proctoscopies. Many of these men become proficient in diagnosis, as any one can by study and close observation. It is unfortunate, however, that the impression still prevails, as it has for a long time in some quarters, that rectal surgery is simple and can be performed satisfactorily by the newest intern. Not only should the surgeon always

have in mind that his object is to remove existing pathologic conditions but he must so conduct the operation that, when healing is complete, there will be no impairment in the function of the parts. The accomplishment of these purposes usually requires a rather exacting technic, equal to that of most abdominal operations. I am confident that there are more unsatisfactory hemorrhoidectomies than appendectomies performed. In the hands of an experienced surgeon, however, a patient has every right to expect, when he submits to an ordinary rectal operation, that he will be completely relieved of symptoms and also that there will be no impairment of function of the parts. Of course, exceptions may occur in cancerous conditions and in some deep and extensive infections. I may add, however, that untoward results are by no means always due to a faulty operative technic. Oftentimes there are other causative factors, and chief among them is lack of proper after-care. Rectal wounds seem to require more attention than those of other parts of the body, and the conscientious surgeon gives them his personal attention unless he has a trained assistant to do this for him.

Often of great concern by the patient who contemplates a rectal operation is the possibility of an incontinence resulting. Loss of control is always to be deplored, of course, but there is little reason for its occurrence except in rare instances. The most common cause of this in the past has been the almost universal custom of forcibly dilating the sphincter muscles as a preliminary step in all rectal operations. This procedure of "paralyzing the sphincters," an expression often employed, was deemed absolutely necessary, particularly if the sphincters were at all spastic. Whether stretching was done with the fingers or with instruments, the muscle fibers often were injured to such an extent that their tone and contractability were destroyed, allowing a leakage to liquid or soft stools. The best informed proctologists no longer dilate the anal canal during any operation unless a fibrous constriction is present.

The postoperative care of a fistula is as important as the operation itself, and not infrequently a failure to cure is due to inadequate attention to the wound. For a time there were some who advocated excision of fistulous tracts with immediate suture. Failure to secure primary union was so common that the method has been abandoned almost entirely. Now it is considered best to leave the tract open to heal by granulation. Until recent years it was thought necessary to keep such wounds tightly packed until healing was complete. This practice has been discarded. It was observed that continuous pressure of the gauze forced apart not only the wound edges but also any muscle fibers which may have been incised. In the healing of a tightly packed wound there will be deposited a wider and more extensive amount of fibrous tissue which, because of its rigidity, necessarily interferes with the normal closure of the sphincters. Incontinence following fistulectomy is more often due to excessive scar tissue than to incised muscles. Of course, adhesions between adjacent raw surfaces must not be allowed to take place, but if such wounds are otherwise left alone the resulting scar will be narrow and interfere little, if at all, with the normal function of the sphincters.

Formerly the so-called "rectal plug" was used regularly by many surgeons on the completion of every rectal operation. This was left in position for several days, the purpose being, it was said, to keep the muscles dilated, prevent adhesions and furnish an avenue of escape for gases. Such a foreign body in the anal canal caused much pain, requiring regular doses of opium to control. Also, when used, retention of urine was a frequent complication. As far as I know, the plug is no longer employed.

The proper interpretation of symptoms and an avoidance of hasty conclusions are necessary in the practice of proctology. Unless one is constantly on the alert there are many possibilities of error. It will be disconcerting, to say the least, to find, shortly after performing a hemorrhoidectomy, that there is a malignant growth only a few inches away. Again, at other times, small symptomless hemorrhoids are removed for pain, bleeding or itching when the symptoms have an entirely different cause. Rarely will a false interpretation be placed on rectal symptoms if a proper and painstaking investigation is made. Errors in diagnosis in this region are usually inexcusable, for most of them are due to carelessness.

When a perirectal abscess is incised the physician, for his own protection if for no other reason, should inform the patient that such an abscess is the first stage of a fistula and that a chronic draining sinus is likely to ensue; also, in all probability, a removal of the sinus or fistula will be necessary before relief is obtained. Too often, if reports are true, attempts are made to cure these tracts by irrigation, cauterization or packing. Such treatment is time consuming and always disappointing.

Every one at all interested in proctology should be familiar with the work of Dr. George Thiele of Kansas City. His contribution, in my opinion, is the most valuable given in our field during the past decade. I refer to a paper read by him [1] in this section and published in THE JOURNAL about five years ago, in which he called attention to spasm of one or more of the deep pelvic muscles causing symptoms previously not satisfactorily explained. The muscles involved are the coccygeus, pyriformis or levator ani, and their spasticity usually may be detected by palpation. Symptoms associated with this condition are somewhat variable, most often a feeling of pressure in the rectum or a dull aching, neuralgic in character, which sometimes extends to the vagina. Systematic and regular massage of the affected muscles, as suggested by him, gives relief in most instances. We have been pleased to note that frequently an associated coccygodynia and low back ache disappear also after massage of these muscles. Apparently no cause for this spasticity has been determined.

Most proctologists are conservative and attempt operations of only the most minor nature in their offices. Surgery of any magnitude is best done in a hospital where suitable assistance is obtainable and conditions in every respect more favorable. I am confident that often too much is undertaken in the office, particularly by young men with limited experience. Only one or two uncontrollable hemorrhages will suffice to convince any one that there are distinct limitations to office surgery. On the contrary, however, the well trained proctologist treats many ailments satis-

1. Thiele, G. H.: Coccygodynia and Pain in the Superior Gluteal Region, J. A. M. A. **109:** 1271 (Oct. 16) 1937.

factorily in his office. Here, again, his knowledge of pathology usually will allow him to differentiate rather accurately whether a condition requires surgery or can be relieved by nonsurgical methods. There are borderline cases which treatment will benefit but not cure completely. In such instances surgery is advisable unless contraindicated because of age or physical disability.

The ambulatory treatment of hemorrhoids has become very popular in recent years. I fear that its limitations are not always understood. Only simple, uncomplicated, internal hemorrhoids are suitable for treatment by the electric needle or by injection of any one of the popular sclerosing agents. Surgery is indicated in all forms of hemorrhoids when associated with other diseases, as cryptitis, papillitis or fistula.

At present most surgeons employ the so-called ligature method in removing hemorrhoids. This seems altogether the most satisfactory and is followed by fewer complications than others. Some still use the clamp and cautery, although usually this causes more pain, and in healing there is deposited a greater amount of connective tissue; also secondary hemorrhages are more frequent. The Whitehead operation, very popular in some sections a few years ago, is almost obsolete now. Theoretically it was considered the perfect operation, but the end results in many instances were far from satisfactory.

Postoperative treatment in rectal surgery has changed materially in recent years. Unless there are unusual complications, soft diet is allowed the morning after operating. In forty-eight hours a bowel movement is secured by either a mild laxative or an enema, following which the patient is given general diet and is allowed out of bed ad libitum. Even within a few hours after operation he may be permitted to stand if there is difficulty in voiding. In allowing this no harm has been observed, but often retention and catheterization, always objectionable complications, may be avoided. Hot sitz baths and hot compresses add much to the comfort of the patient and are conducive to healing. Unless the operation has been extensive or an unusual one, the patient leaves the hospital in four to six days. He is requested to report to the office regularly every few days until healing is complete. At these visits any tendency to adhesions or bridging of the wounds is forestalled and excessive granulation tissue removed. Success or failure of operations on the rectum is more often dependent on the amount and nature of the aftercare than is generally admitted.

Many surgeons have reported favorable results from topical applications of the sulfonamides to open postoperative wounds. It has been my experience that their use has not reduced noticeably the time of healing, and in no way have they seemed superior to the mild antiseptic wet dressings and sitz baths which have been employed for many years. These drugs, however, administered internally are most effective and indispensable in many deep seated infections. In addition, certain of them are more or less specific in many cases of ulcerative proctitis. All drugs of this class are dangerous and should not be prescribed indiscriminately. For myself, when I think they are indicated I prefer that they be administered by and under the close supervision of an internist or a gastroenterologist. The medical practitioner is better able to keep a close watch and detect in their incipience any untoward effects, should they arise. In fact, there should be a close cooperation between the gastroenterologist and the proctologist. There are innumerable occasions in which they may be of mutual benefit.

Most of us are more or less creatures of habit. We often prescribe remedies or employ methods handed down from one generation to another without consideration as to their merits. One in particular is the custom, in some localities at least, of prescribing ointments and suppositories containing opium for inflamed and painful conditions at or near the anal outlet. Few drugs are absorbed through the unbroken skin. Opium is not a local anesthetic and, when applied or inserted into the rectum, can relieve pain only after it is absorbed into the blood stream. A mild antiseptic wet dressing with a hot water bag over it is generally more effective than any ointment or suppository. Most of the popular ointments and suppositories owe their reputation to the fact that they are used generally in acute, self-limiting diseases.

The physician should discourage the indiscriminate use of laxatives. One is sometimes surprised how quickly a sluggish and inactive bowel will respond to simply a regulation of diet and habits, when the patient is fully cooperative. Frequently, however, some aid other than laxatives is necessary. For this purpose preparations containing seed taken in 1 to 2 teaspoon doses daily are very effectual in many instances. They seem not to have any of the detrimental effects of liquid petrolatum, which for many years has been used extensively in chronic constipation. Oil interferes with digestion, prevents proper assimilation of food and prevents absorption of certain vitamins. The taking of oil, except for a very limited time, should be discouraged.

Some physicians make it a rule to order a roentgenoscopy whenever cancer of the lower bowel is suspected. A tumor located in the ampulla of the rectum often is not diagnosed definitely by the x-rays. When the report is found to be inconclusive, a proctoscopy is requested. The procedure should be reversed. If a growth is located through the proctoscope a biopsy specimen will determine the diagnosis definitely. Then roentgenoscopy is generally not necessary.

We are passing through an era of great progress in medicine. Proctology has kept pace with all other progressive departments of medicine and probably is ahead of some. These accomplishments have been the result of contributions of many interested, hard working and observant individuals. We have by no means, however, reached the stage of perfection. That new ideas and improved methods will continue to be brought forth from time to time there is no reason to doubt; that is, while we remain free and independent agents. When, however, the practice of medicine becomes regimented, as is strongly advocated in certain quarters, most certainly progress will be at an end. Then medicine will be practiced carelessly and indifferently.

One cannot imagine that physicians of today will tolerate the dictatorship of a centralized group of selfish and autocratic politicians, whose chief interest is not that of their dear constituents, as they claim, but that of feathering their own political nests.

116 East Franklin Street.

CHRONIC GLOMERULONEPHRITIS AND THE NEPHROTIC SYNDROME

A FOLLOW-UP INVESTIGATION OF PATIENTS TREATED WITH ACACIA

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"It is indeed an humiliating confession that although much attention has been directed to nephritis for nearly ten years—yet little or nothing has been done toward devising a method for permanent relief, when the disease has been confirmed; and no fixed plan has been laid down as affording a tolerable certainty of a cure in the more recent cases." Richard Bright [1] wrote the foregoing in 1836. In 1944 we still must confess that we cannot cure the patient who has this disease, but the plan of treatment [2] here to be described restores many of the patients to work and eases the sufferings of those who are bedfast.

Our purpose in this study was to ascertain the health of the patients and the status of the disease from which they suffered in the interval between the time of their first treatment at the Mayo Clinic and the time of the follow-up investigation. At the time of admission at the clinic the 109 patients selected for study had in common glomerulonephritis and the nephrotic syndrome, extensive and resistant edema, and they were treated with injections of a solution of acacia in the years 1937 to 1943 inclusive. By "nephrotic syndrome" is meant the clinical state characterized by albuminuria, the presence of edema and a decreased concentration of serum albumin. In addition, the concentration of blood cholesterol usually is elevated and not infrequently the basal metabolic rate is lowered. Two of the 109 patients, in addition, received diagnoses of Hodgkin's disease; 1 other patient had indeterminate edema and 1 chronic hepatitis. Of the 109 patients, 72 were alive and 25 were dead at the time of the follow-up investigation; we received no response concerning 12. Of the 72 patients known to be living, 27 were more than 40 years of age at the time when data for this report were gathered.

Glomerulonephritis with nephrotic tendencies is primarily a disease of children and young adults. Grouped according to decades of life, most of the patients were in their teens when the symptoms became evident and the next largest number were in the third decade of life. Three patients were less than 10 and 2 were more than 68 years of age. The exact age of the onset is difficult to determine because patients without extrarenal symptoms frequently do not go to a physician. It has been said [3] that even now in the majority of instances the presence of Bright's disease remains unsuspected and that only a small proportion of all people with this disease ever lie on a postmortem table or even in a hospital bed. Most of our patients had had symptoms of renal disease for three to four years when first seen at the clinic; in 5 of the cases the kidneys had been known to be involved longer than ten years and in 2 of them longer than eighteen years. Males seem to be more susceptible to the disease than females. In our series of 72 patients who could be followed up 39 were men and 33 women.

These patients complain chiefly of malaise and of discomfort from the edema. In a severe case the legs are so swollen that to walk is troublesome. Swelling of the genitalia may make urination difficult and painful; edema of the abdominal wall and ascites cause distention, impede respiration and cause slowing of gastric motility; pleural effusion causes dyspnea and may embarrass the circulation; edema of the stomach and intestine causes loss of appetite, indigestion, nausea, vomiting and intestinal irregularity; cerebral edema may cause headache, mental confusion, lethargy and possibly psychosis. All but 3 of the group of 109 patients had edema, varying from pitting edema at the ankles, sometimes extending upward to the knees or hips, to generalized anasarca with fluid in the body cavities. Forty-two patients had clinically demonstrable fluid in the pleural or peritoneal cavities.

Our plan of treatment is directed toward removing the edema and helping to restore the normal concentration of serum protein. Dietary aids consist in restriction of intake of sodium and protection of the normal concentration of serum protein. Patients are instructed to take either a salt free diet or one containing only the salt used in preparation of the food. Intake of fluids is limited to not more than 1 to 1½ quarts (approximately 1 to 1.5 liters) daily. The protein content of the diet is increased to between 75 and 125 Gm. daily because of the excessive proteinuria that is one feature of the nephrotic syndrome. There is no evidence that forced injection of protein produces a significant rise in the concentration of serum protein, although it may prevent progress of hypoproteinemia. Vitamins and iron may be used to supplement the diet. Potassium nitrate is used indefinitely in a dose of 3 Gm. three times daily. This diuretic drug has low toxicity, is easily administered and has the desired diuretic action. Administration of acacia is indicated when renal function is good, the concentration of serum protein is low and the edema does not respond readily to treatment in the hospital. The usual total dose is 90 Gm.; that is, a 6 per cent solution of pure acacia in 1,500 cc. of a 0.06 per cent solution of sodium chloride. One third of this quantity is given in each of three intravenous injections administered usually on alternate days. In the average case in which the intake of fluid is controlled, this quantity will give a concentration of approximately 2 Gm. of acacia per hundred cubic centimeters of blood serum. It it fails to give this concentration or if clinical edema is still present, further injection can be given. Mercurial diuretic drugs may be more effective after administration of acacia than before.

The acacia is gradually eliminated from the blood. One year after the administration the average concentration is 100 mg. per hundred cubic centimeters of serum. Power [4] has reported 25 mg. per hundred cubic centimeters being found in the serum three years after the last injection. The concentration of acacia in the blood serum of 1 patient who recently returned for reexamination six years after her last injection of acacia was 10 mg. per hundred cubic centimeters.

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1. Bright, Richard, cited by Loeb, R. F.: Nephritis (Bright's Disease), in Cecil, R. L.: Textbook of Medicine, ed. 5, Philadelphia, W. B. Saunders Company, 1940, p. 1018.

2. Goudsmit, Arnoldus, Jr., and Binger, M. W.: Treatment of Nephrotic Edema, J. A. M. A. **114**: 2515-2517 (June 29) 1940. Lehnhoff, H. J., Jr., and Binger, M. W.: Treatment of Edema of Renal Origin: Report of Twelve Cases, ibid. **121**: 1321-1325 (April 24) 1943.

3. Addis, Thomas, and Oliver, Jean: The Renal Lesion in Bright's Disease, New York, Paul B. Hoeber, Inc., 1931, p. 15.

4. Power, M. H.; Keith, N. M., and Wakefield, E. G.: The Persistence of Acacia in the Blood After Intravenous Injection of Acacia Solution, Am. J. Physiol. **113**: 107 (Sept.) 1935.

She had received the average total dose of 90 Gm. of acacia. Twenty of the 25 patients who were dead at the time of the follow-up investigation had lost their edema when hospitalized at the clinic under treatment which included administration of acacia. Twelve [4] of the 25 patients lived two years or longer after returning home. Five patients lived four years or longer. The listed causes of death were further manifestations of chronic Bright's disease, such as uremia, hypertension and cardiac failure in most of the cases; also acute appendicitis, mastoiditis, pancreatitis, septicemia and old age were reported.

We now propose to discuss certain manifestations of this disease, found at the initial examination and either at reexamination or at the time of the follow-up inquiry of the 72 living patients.

Of this number, at the time of the follow-up investigation 49 were doing a full day's work—substantial work as business executives, stenographers, farmers, housewives and students. One woman was teaching school in addition to caring for her house and family. Two patients were only slightly handicapped, 19 were working part time, at least half a day, and 2 were bed patients. One of the latter was a man 74 years of age.

Administration of acacia was instituted 103 times with reference to these 72 patients, and 342 separate injections were given. Most patients received 90 Gm. of acacia distributed in three injections; however, 1 patient has received nineteen injections, or 570 Gm., and 12 have received more than 200 Gm. No ill effects have been reported.

In 12 cases reactions occurred in the course of administration of the acacia. They consisted of coldness of the extremities, flushing of the face, chill,[5] nausea, vomiting, dyspnea and urticaria. Two of these 12 patients had reactions two and three times, but all the patients were able to complete the necessary injections, including 1 patient with a proved allergy. In some instances epinephrine was given in the solution prophylactically to patients who had had one reaction, and this prevented recurrence.

Nephrotic edema may develop at any time during the course of the disease. One patient was relieved of clinical edema sixteen years after onset of the disease and 2 others twelve and eight years respectively after the disease began. Acacia was given to these 3 patients on one or two different occasions. All were working when this was written. Acacia was administered to these 72 patients at least two years, and to some of the patients seven years, before the time of this report. The mode of action of acacia is not certain, but it does facilitate excretion of sodium chloride and water.[6] The value for blood chlorides was elevated on primary admission in most of the cases in which the value was determined. Once the excretion of sodium ion is initiated, edema fluid is restored to the circulation and then is eliminated by way of the kidneys. Under treatment, all 72 patients lost weight with the diuresis and with the decrease in edema. The average loss of weight was approximately 19 pounds (8.6 Kg.) per patient. Twelve patients lost 30 pounds (13.6 Kg.) or more and 3 lost 46, 55 and 60 pounds (20.9, 24.9 and 27.2 Kg.) respectively. On the average, 1 to 2 pounds (0.5 to 0.9 Kg.) is lost daily.

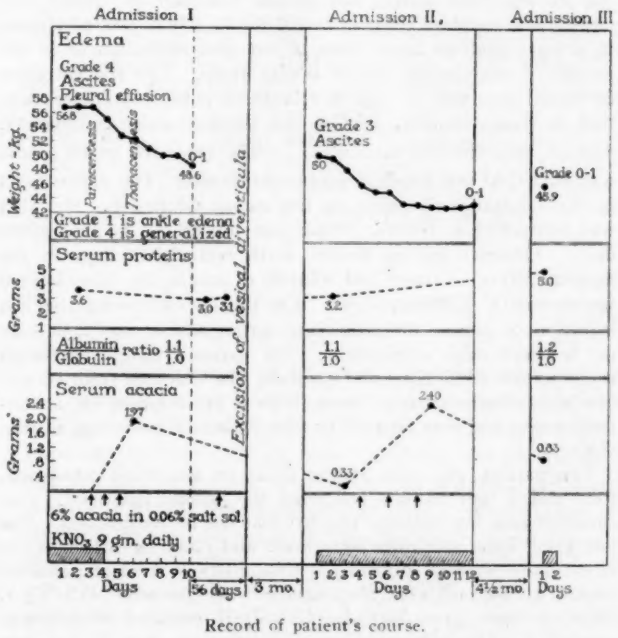
5. Goudsmit, Arnoldus, Jr.; Power, M. H., and Bollman, J. L.: Some Effects of Injection of Acacia, with Special Reference to Renal Function, Proc. Soc. Exper. Biol. & Med. **47**: 254-257 (June) 1941.

6. Goudsmit, Arnoldus, Jr.; Binger, M. W., and Keith, N. M.: Acacia in Treatment of the Nephrotic Syndrome, with Special Reference to Excretion of Chloride and Water; a Report of Cases, Arch. Int. Med. **68**: 513-524 (Sept.) 1941. Goudsmit, Power and Bollman.[5]

The normal concentration of serum proteins is 6 to 8 Gm. per hundred cubic centimeters [7] and the normal albumin-globulin ratio $\frac{1.5 \text{ to } 3.0}{1}$. Among 38 patients reexamined after administration of acacia on a previous visit the value for total serum proteins of 30 was found to have increased. In addition the albumin-globulin ratio of 2 had become normal. Clinically, 15 patients of this group of 38 had had ascites or demonstrable pleural fluid in addition to the peripheral edema at the time of the first admission but not at reexamination. Also 33 of the 38 patients had no edema or minimal edema of the ankles only at the time of the last admission, while all of them had exhibited considerably more edema than this when first seen at the clinic.

What has just been said about edema, serum acacia and serum proteins is illustrated in the following report of a case:

A woman aged 60, who was admitted to the clinic Sept. 26, 1941, stated that for five years she had had frequency, nocturia and dysuria without chills, fever or colic. Six weeks before she came to the clinic, while on a trip and after she had waded in



Record of patient's course.

a cold stream, a cold had developed and at that time the patient first had noticed swelling of her ankles and legs. This condition had progressed until her abdomen had begun to swell ten days before her admission.

On examination the legs were found to be decidedly edematous and the edema extended upward to include the sacral and lumbar regions. She had ascites as well as effusion in both sides of the thorax, as shown in the accompanying chart. She weighed 125 pounds (56.8 Kg.). The blood pressure was normal and results of examination of the ocular fundi were essentially negative. Urinalysis revealed a specific gravity of 1.019, albuminuria graded 4 and pus graded 1. The blood contained 26 mg. of urea per hundred cubic centimeters and 3.6 Gm. of serum proteins. The albumin-globulin ratio was $\frac{1.1}{1.0}$. An intravenous urogram revealed multiple vesical diverticula, one of which contained a stone. The vesical findings were thought to account for the local urinary symptoms. A diagnosis was made of chronic glomerulonephritis with nephrotic features, and vesical diverticula with stone.

The patient was in the hospital sixty-five days after her first admission. At once a diet was prescribed which was free of

7. Peters, J. P., and Man, E. B.: The Interrelations of Serum Lipids in Patients with Diseases of the Kidneys, J. Clin. Investigation **22**: 721-726 (Sept.) 1943.

salt, high in protein and high in calories and of which the quantity of fluid was controlled. As a diuretic measure, administration of potassium nitrate in a dose of 9 Gm. daily was started but had to be discontinued after four days because of nausea. On the patient's third day in the hospital abdominal paracentesis was performed, and 1,200 cc. of fluid was removed. On the sixth day in the hospital 500 cc. of clear fluid was aspirated from the right side of the thorax. On each of the third, fourth and fifth days in the hospital injections of 500 cc. of 6 per cent solution of acacia were given intravenously, in all 1,500 cc., containing 90 Gm. of acacia. On the day following the last injection the concentration of serum acacia was 1.97 Gm. per hundred cubic centimeters. On the patient's tenth day in the hospital her weight was 107 pounds (48.6 Kg.) and her condition was improved enough to warrant surgical treatment for the vesical diverticula and stone. The postoperative course was essentially uneventful but, because edema of the ankles and legs developed, a fourth intravenous injection of 500 cc. of 6 per cent solution of acacia was given in the fourth postoperative week.

Three months after the patient's dismissal from the surgical service she was readmitted to the hospital because of increasing edema. Examination revealed pitting edema of the legs, including the hips, and ascites was present although the thorax was clear. She weighed 110 pounds (50 Kg.). There was no change in urinary findings from those of her first admission or in the results of examination of the ocular fundi. The concentration of blood urea was 24 mg. per hundred cubic centimeters and that of serum proteins 3.2 Gm. per hundred cubic centimeters. The albumin-globulin ratio was $\frac{1.1}{1.0}$. The value for serum acacia was 0.33 Gm. per hundred cubic centimeters. The patient was in the hospital twelve days on her second admission. Her diet was controlled as before. Potassium nitrate 9 Gm. was given daily. On each of the fourth, sixth and eighth days in the hospital 500 cc. of 6 per cent solution of acacia was administered intravenously, 1,500 cc. in all. On the day following the last injection of acacia the value for serum acacia was 2.40 Gm. per hundred cubic centimeters. The patient's weight decreased to 94 pounds (42.7 Kg.) and clinically she was free from edema. She was dismissed to go home with a prescription for a controlled diet and was advised to take 9 Gm. of potassium nitrate daily.

The patient was seen at the clinic on her third admission, four and a half months following the second dismissal. She came because her husband insisted that she be reexamined. She had been doing her own housework and climbing fifteen stairs twice daily without difficulty. Examination revealed minimal edema at the ankles. She weighed 101 pounds (45.9 Kg.). Blood pressure was normal. Urinalysis revealed albuminuria graded 3. The concentration of blood urea was 26 mg. per hundred cubic centimeters. The concentration of serum proteins was 5.0 Gm. per hundred cubic centimeters and the albumin-globulin ratio $\frac{1.2}{1.0}$. The value for serum acacia was 0.83 Gm. per hundred cubic centimeters. The patient was dismissed to go home and was advised to continue with the same treatment. She wrote us recently that she was getting along well.

Values for blood cholesterol ranging from 129 to 1,190 mg. per hundred cubic centimeters were obtained at the time of first admission of 65 of the 72 patients who later responded to our questionnaire. In 60 of these cases the values were primarily in excess of what we considered the normal of 160 to 200 mg. per hundred cubic centimeters. The values in 47 cases fell between 216 and 595 mg. per hundred cubic centimeters. The 2 patients most seriously ill at the time of writing of this paper had values of 378 and 490 mg. per hundred cubic centimeters. The patients with respectively the very high and the very low values were working and well. When the patients were placed under dietary control, the values for blood cholesterol that had obtained on primary admission fell rapidly toward normal; that is, in 1 case in which the value on primary admission was 595 mg. per hundred cubic centimeters the value became 282 mg. per hundred cubic centimeters eight days later. It was also interesting that in cases in which values for serum protein on primary admission were low frequently hypercholesterolemia was found, while in cases in which values for serum protein were more nearly normal on primary admission the values for blood cholesterol were low. Peters and Man[7] reported that in their series of 54 nephritic patients the hypercholesterolemia bore no consistent relation to any single phenomenon of the disease. They stated that hypercholesterolemia was encountered most frequently in the presence of edema and that it was most striking in cases in which there was the greatest deficiency of serum albumin. From these observations it would appear that the initial value for blood cholesterol has very little prognostic significance.

We used retention of blood urea as an index of renal function in place of the urea clearance test because of the poor urinary output of this group of patients. This value is obtained by multiplying the value for urea nitrogen by the factor 2.14. The normal value ranges between 15 and 40 mg. per hundred cubic centimeters. On their first admission 26 of the 72 patients gave evidence of some renal insufficiency, as shown by elevation of the concentration of blood urea. These 26 patients had been known to have renal disease for from two to nineteen years, the majority for from two to nine years. The value returned to normal in 4 of these cases while treatment was being given in the hospital following the primary admission. In 8 more cases the values obtained on primary admission were decreased but were still above normal limits at the time of dismissal. The concentration of blood urea in 3 of the 8 cases later returned to normal. Also in 3 of the 26 cases the value for blood urea was elevated on primary admission, rose still higher while treatment was being given and was still elevated on dismissal; the value had returned to normal, however, at a later reexamination. This makes a total of 10 of these 26 patients whose measurable renal insufficiency evidently improved sufficiently to reach normal either while under treatment at the clinic or after their dismissal.

Four of the 72 patients had had the disease eleven years or longer. The values for blood urea were normal when they were first examined. The concentration of the blood urea of a fifth patient on primary admission, who also had had the disease eleven years or longer, was elevated to 46 mg. per hundred cubic centimeters.

Nine of the 72 patients had blood urea of normal concentration at the time of the first admission but gave evidence of renal insufficiency on reexamination. All 9 patients had had the disease from two to eight years when this elevation in value for blood urea was noted. In 4 of these 9 cases hypertension was an associated condition and, in all, apparently the hypertension was progressive.

We took 4,250,000 to 5,250,000 per cubic millimeter of blood as the normal erythrocyte count. For females 13 to 16 Gm. per hundred cubic centimeters of blood, and for males 14 to 17 Gm. was taken as the normal concentration of hemoglobin. By the foregoing standards 43 of the 72 patients were anemic on primary admission. Anemia finally develops in most cases of chronic nephritis. The lowest erythrocyte count was 2,040,000 and the lowest hemoglobin determination was 6.8 Gm. per hundred cubic centimeters. The leukocyte counts of 23 patients were increased when they were

first admitted; the highest leukocyte count was 16,200 per cubic millimeter of blood. By the foregoing standards, of the 38 patients later reexamined 8 who previously had been anemic gave normal values at reexamination; however, on reexamination 6 patients were anemic who had not been anemic on primary admission. The treatment of anemia in the presence of chronic nephritis is difficult.

Of 29 patients whose basal metabolic rates were estimated, 9 gave readings of more than — 10 per cent on primary admission. In no case was the rate more than + 10 per cent. The basal metabolic rates of 2 patients were — 25 and — 37 per cent. Also the blood cholesterol values of both of these patients were elevated respectively to 893 and 1,190 mg. per hundred cubic centimeters. The laboratory picture, therefore, resembled that seen in myxedema. Desiccated thyroid was used as an adjunct in treatment of these 2 patients. Both were working part time when this report was written.

Using determinations of blood pressure of 150 mm. of mercury systolic and 90 mm. of mercury diastolic as arbitrarily taken upper limits of normal, 27 of 38 patients who were reexamined had normal blood pressures at the time of the reexamination. Seven of these 27 patients had had hypertension at a previous visit. At the time of reexamination, hypertension was present in the 11 remaining cases of the 38. In 6 of these 11 cases the hypertension apparently had developed since the previous visit, while in the other 5 cases it had been present at a previous visit and had continued. The patients with hypertension represented all decades of life from the teens to the seventies. They had had renal disease for from two to nine years when hypertension developed; this period of antecedent renal disease is like that encountered in the cases of renal insufficiency. Four of the 11 patients with hypertension complained of exertional dyspnea and 4 of headache. These two groups of 4 overlap. This type of headache usually is frontal, is present in the early morning, on awakening, and usually lasts one to two hours.

Two of the 72 patients, both men, aged 18 and 24 years respectively, presented the ophthalmoscopic picture of developing retinitis.[8] One had had knowledge of his renal disease for eight years and the other for two years. Also in both cases hypertension and nitrogen retention had developed since the patients first had been examined at the clinic. They both continued to have some clinical edema.

Retinitis at times may be reversible. In the ocular fundi of 4 patients were signs indicating regression of previous retinitis. Two of these patients, whose blood pressures had been elevated when they first had been seen at the clinic, had normal blood pressures at the time of their last visits. Slight nitrogen retention was found in examination of 3 of these 4 patients when they were last examined.

Using the microscopic evidence of erythrocyturia, leukocyturia and cylindruria, and the presence of albuminuria as criteria, 20 of the 38 patients reexamined gave evidence of improvement in urinary findings on reexamination; 11 of these patients showed some improvement, 5 showed definite improvement and the urine of 4 was normal. These studies of the urinary sediment indicate that at the time of these examinations the disease was relatively quiescent but, as Addis and Oliver [9] and Christian [10] have pointed out, qualitative observations of the urinary sediment are only now and then decisive and are not prognostic.

In all cases in which values for plasma fibrinogen were determined, the results were within the normal limits of 300 to 600 mg. per hundred cubic centimeters. A tendency to bleeding was not exhibited by any patient following the use of acacia.

This follow-up study indicates that many of the patients who had resistant nephrotic edema and who were treated successfully with acacia and other treatments discussed have been able to maintain a more nearly normal economic and social existence than they had been able to lead before treatment. As was said in an earlier paragraph, we could not find any evidence that acacia was harmful in any way to these patients.

8. Keith, N. M.; Wagener, H. P., and Barker, N. W.: Some Different Types of Essential Hypertension: Their Course and Prognosis, Am. J. M. Sc. **197**: 332-343 (March) 1939. Graham, R. W.: Ophthalmoscopically Visible Retinal Lesions in Chronic Glomerulonephritis: Occurrence and Characteristics, Arch. Ophth. **26**: 435-465 (Sept.) 1941.

9. Addis and Oliver: The Renal Lesion in Bright's Disease,[3] pp. 18 and 19.

10. Osler, William: Principles and Practice of Medicine, revised by H. A. Christian, ed. 13, New York, D. Appleton-Century Company, Inc., 1938, pp. 867-868.

SEPTICEMIA AND BACTERIAL ENDOCARDITIS RESULTING FROM HEROIN ADDICTION

REPORT OF FIVE CASES

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The development of bacterial infection of the blood stream in narcotic addicts as a result of their addiction is a rare occurrence. This is somewhat surprising in view of the fact that so many addicts use morphine or heroin by injection and entirely without antiseptic technic. Most [1] has reported on the epidemiologic and clinical aspects of more than 200 cases of malaria in drug addicts in New York City. Apparently this disease is not uncommon, being spread through groups of addicts as a result of contamination of their injection equipment with blood containing the parasites. This assumption is based on the fact that it is common practice for addicts to employ a single syringe and needle for a series of injections in different individuals without the slightest attention to cleansing of the equipment between injections. Doane [2] reviewed the literature on the subject of tetanus acquired by narcotic addicts presumably as the result of using contaminated equipment for injection. He added 3 cases to the total of 9 cases previously reported by other authors. In addition, there have been several reports [3] on the occurrence of

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1. Most, H.: Falciparum Malaria Among Drug Addicts: Epidemiologic Studies, Am. J. Pub. Health **30**: 403 (April) 1940; Falciparum Malaria in Drug Addicts: Clinical Aspects, Am. J. Trop. Med. **20**: 551 (July) 1940.

2. Doane, J. C.: Tetanus as a Complication in Drug Inebriety, J. A. M. A. **82**: 1105 (April 5) 1924.

3. Wikler, A.; Williams, E. G.; Douglass, E. D.; Emmons, C. W., and Dunn, R. C.: Mycotic Endocarditis, J. A. M. A. **119**: 333 (May 23) 1942. Wikler, A.; Williams, E. G., and Wiesel, C.: Monilemia Associated with Toxic Purpura, Arch. Neurol. & Psychiat. **50**: 661 (Dec.) 1943.

blood stream infection by Monilia in drug addicts, and in 3 cases mycotic endocarditis was found.

Over a period of about a year we have observed 5 cases of septicemia in heroin addicts, 4 of whom had acute bacterial endocarditis. Because the development of septicemia under these circumstances is unusual, these cases are reported here in detail.

REPORT OF CASES

CASE 1.—A man aged 45, Chinese, was admitted to the Psychiatric Division of the Gallinger Municipal Hospital for the treatment of heroin addiction of several years' standing. Because of language difficulties it was impossible to obtain an adequate history. He appeared acutely ill and had labored respirations. The blood pressure was 140/70, temperature 101 F., pulse rate 100 and respiratory rate 36. There were many needle puncture marks along the veins of both upper extremities. Several infected ulcers were present over the middle third of the left tibia. Three petechiae were visible in the left palpebral conjunctiva. Over the lower half of the right lung there were found diminished tactile fremitus and impaired resonance. Bronchovesicular breathing and subcrepitant rales were heard in this same area. A soft, nonradiating, apical systolic murmur could be heard. His abdomen was distended and tympanitic. Urinalysis showed 2 plus albumin, 2 granular casts and 18 red cells per high power field. The red blood cell count was 2,630,000, the white blood cell count 25,000 with 80 per cent polymorphonuclears, 13 per cent young forms, and 7 per cent lymphocytes. Type XXIV pneumococcus was found in the sputum. A blood culture taken on admission was negative.

Sulfathiazole was started on admission, and adequate levels were obtained. An x-ray film of the chest on the second hospital day showed diffuse pneumonitis in the lower half of the right lung. There was no apparent change during the ensuing two weeks except for the appearance of several petechiae on the hands and feet. His temperature fluctuated between 99 and 104 F. Severe chills occurred almost daily, but blood cultures were repeatedly negative. The white blood cell count remained elevated.

On the fifteenth hospital day sulfathiazole was discontinued and sulfadiazine started. An x-ray film of the chest showed some clearing of the pneumonitis at the right base. The chills continued, however, and on the sixteenth, seventeenth and eighteenth days positive blood cultures were obtained by another laboratory and Bacillus pyocyaneus was grown. New petechiae appeared on the chest and extremities, and the patient looked more severely ill and irrational. There was no change in the character of the temperature curve. On the nineteenth hospital day a short, high pitched early diastolic murmur of low intensity was heard in the second left intercostal space next to the sternum.

The remainder of the clinical course was steadily downhill. There were no significant alterations in the physical and laboratory findings. In view of the reported beneficial effects from the use of acetic acid in the treatment of B. pyocyaneus infection of the skin, and because the sulfonamides had shown no ameliorating influence on the disease in this case, 100 cc. of 1 per cent acetic acid solution was given by vein daily for five days. There was no observable effect from this treatment. The patient died on the thirty-ninth hospital day.

At necropsy the heart weighed 620 Gm. and was moderately dilated. The pericardial cavity was completely obliterated as the result of fibrinous pericarditis. The heart valves were normal except for a large, soft friable vegetation on the anterior cusp of the aortic valve. Just above this leaflet there was a mycotic aneurysm 3 cm. wide and 2 cm. deep. A culture of the vegetation was positive for B. pyocyaneus. The spleen weighed 350 Gm., was quite firm and contained 3 infarcts. There were also numerous small infarcts in the kidneys.

CASE 2.—C. S., a Negro aged 38, was admitted to the hospital because of cough and loss of weight. His illness had begun three months before admission with cough, anorexia and night sweats. On the advice of a friend the patient began taking heroin intravenously as a tonic. The drug had been administered daily by vein without use of antiseptic precautions of any kind. During the three months he had lost 18 pounds (8 Kg.) in weight. Just prior to admission he had become weak, dyspneic and febrile. A roentgenogram of the chest taken one week before admission had been reported as negative.

On examination the patient looked acutely ill and dyspneic. The temperature was 102.5 F., pulse 125, respiratory rate 32, blood pressure 110/68. The forearms showed scars along the veins at the sites of injection of heroin. The breath sounds were diminished and there were subcrepitant rales over the posterior aspect of the left lung at the base. The remainder of the physicial examination was negative.

The urinalysis was normal. There were slight leukocytosis and mild anemia. An x-ray film of the chest showed areas of increased density in the lower half of the left lung and a slight increase in the transverse diameter of the heart. A blood culture taken on the third hospital day was reported to show Staphylococcus albus, but several subsequent cultures yielded Staphylococcus aureus which was coagulase positive. An x-ray film of the chest made on the seventh day revealed discrete areas of soft infiltration containing radiolucent centers scattered throughout both lungs.

The patient was given sulfamerazine, and adequate blood levels were maintained. His course was septic and rapidly downward. On several occasions he coughed up blood tinged sputum. Except for the development of rales in additional areas of the lungs, there were no new physical findings. The white blood cell count ranged between 18,000 and 21,000. He died on the fourteenth hospital day.

At necropsy the heart weighed 325 Gm. The valves were normal except the tricuspid, which was the site of a large mass of soft vegetations. Both lungs contained innumerable small abscesses of embolic origin. Cultures from the vegetations and from the lung abscesses yielded Staphylococcus aureus. The spleen was moderately enlarged.

CASE 3.—O. B., a Negro woman aged 25, was acutely ill when admitted to the hospital, and her history was vague. She was about six months pregnant and had been well until a few weeks before admission. Then she had developed fever, vomiting and symptoms of a respiratory infection, including sore throat and cough. Six days prior to admission she had anointed her skin first with alcohol and then with camphorated oil for relief of headache. The next day blebs had appeared on her skin, and the following day peeling had begun.

The patient looked stuporous and seriously ill. The temperature was 102.5 F., pulse 130, respiratory rate 48, blood pressure 120/70. The face was swollen, and there was extensive patchy exfoliation of the skin of the arms and chest with many cracked and bleeding areas. On the arms were several flattened bullous lesions. The mucous membranes and tongue were dry, and the pharynx was congested. At the base of the right lung resonance was diminished, and there were subcrepitant rales in both axillas and at the right base. The heart was normal in size. There was a short soft systolic murmur on the left of the sternum and a gallop rhythm. The uterus was enlarged to the level of the umbilicus. The fetal heart sounds were distinctly audible. Extensive raw areas were seen around the vulva.

Urinalysis showed albumin (1 plus), there was moderately severe anemia and the leukocyte count was 20,500. A blood culture taken on the first day yielded Staphylococcus aureus, and this organism was repeatedly obtained. The blood urea nitrogen was 16 mg. per hundred cubic centimeters. An x-ray film of the chest showed soft areas of infiltration scattered throughout both lung fields suggesting pulmonary infarcts.

The patient lived nine days after entering the hospital. She was treated with sulfamerazine for two days and then with

penicillin until the time of her death. The hematologic and bacteriologic findings remained the same, but the patient's general appearance improved temporarily after penicillin was started. High fever and tachycardia continued, however, and after the sixth day she became rapidly weaker. The fetal heart sounds were last heard on this day.

After she died it was learned from the patient's husband that she had been addicted to the use of heroin administered intravenously without aseptic precautions.

At necropsy the heart weighed 320 Gm. There were 3 gray, warty vegetations on the tricuspid valve. The other valves were not affected, and none of the valves showed evidence of preexisting disease. The peripheral parts of the lungs were filled with numerous small septic infarcts, many of which had formed abscesses. The liver was greatly enlarged as the result of cloudy swelling, and the spleen was slightly enlarged.

CASE 4.—A Negro aged 33, the husband of patient 3, was admitted to the hospital because of an abscess of the left antecubital fossa and for diabetic control. The patient had administered heroin to himself at irregular intervals by the intravenous route for seven years. However, for the preceding three months he had used the drug three times daily. Sterile precautions were not observed at any time, and on several occasions abscesses had developed at the sites of injection. The infection of the left antecubital space had been present for about a week. He stated that he and his wife used the same syringe and needle.

The only significant findings on examination included many scars along the veins of both upper extremities and an area in the left antecubital fossa which was swollen, warm, red, tender and firm. The temperature was 102 F., pulse 110, respiratory rate 20 and blood pressure 130/80.

Urinalysis showed 4 plus reduction of Benedict's solution. The red blood cell count was 4,270,000, the white blood cell count 11,300. The blood sugar was 400 mg. per hundred cubic centimeters. A blood culture taken on admission was negative. An x-ray film of the left elbow showed no evidence of bone or joint disease.

After two days of application of hot saline soaks to the area of cellulitis the patient's temperature returned to normal and the inflammation appeared to be subsiding. On the seventh and ninth days his temperature rose to 100 F. and on the eleventh day he had a severe chill with a rise in temperature to 103 F. His temperature remained elevated and fluctuated between 99 and 103 F. for the ensuing five days, during which time three positive blood cultures for Staphylococcus aureus were obtained. At this time the patient looked acutely ill and complained of profound weakness and severe generalized aches and headache. Sulfamerazine was started and adequate levels maintained. The temperature gradually fell to normal during the next six days and the patient appeared much improved. Three positive blood cultures for Staphylococcus albus were reported for this period. The local infection in the antecubital fossa became fluctuant and was incised. A small amount of pus containing Staphylococcus aureus was evacuated. Sulfamerazine was discontinued at this time and penicillin administered by the intramuscular route for the next seven days. No further positive blood cultures were obtained. The patient continued to improve, and the incision healed completely. Diabetic control was unsatisfactory during the first three weeks of hospitalization but was well established from then until his discharge on the fifty-fourth hospital day.

CASE 5.—F. N., a Negro woman aged 28, entered the hospital complaining of pain in the upper half of the left hemithorax. Ten days before admission she had experienced chilliness followed by a feeling of fever. These symptoms had recurred repeatedly each day afterward. After four days she had suddenly been stricken with sharp pain in the left pectoral region. Cough had then begun and had noticeably aggravated the pain. Her private physician had informed her that she had pleurisy, and sulfathiazole had been prescribed. The cough later had become productive of thick brown sputum.

The patient had been taking heroin intravenously for four months, during which time there had been a loss in weight of 50 pounds (23 Kg.). The syringe and needle used for injections had not been sterilized at any time.

On examination the patient looked acutely ill and emaciated. The temperature was 102.8 F., pulse rate 110, respiratory rate 32 and blood pressure 100/75. Both forearms were scarred along the course of the veins. There were bronchovesicular breath sounds and suberepitant rales over the left upper lobe. The heart was normal except for a soft apical systolic murmur.

Urinalysis showed a trace of albumin. There was moderately severe anemia, and the leukocyte count was 6,400 with 75 per cent neutrophils and 25 per cent lymphocytes. Smears for malaria were negative. X-ray examination of the chest showed small areas of infiltration in the left upper lobe. Blood cultures were repeatedly positive for Staphylococcus aureus.

The patient lived thirty-one days after entering the hospital. Her clinical course was septic and steadily downward. She was treated with sulfamerazine without any effect on either the course or the positive blood cultures. Subsequent x-ray films of the chest demonstrated clearing of the infiltration in the left upper lobe and the appearance of numerous new areas of involvement which were interpreted as pulmonary infarcts. From time to time there was expectoration of fresh blood, but the physical findings in general were not altered except for variation in the location of pulmonary rales.

At postmortem examination the heart was not enlarged. There was acute bacterial endocarditis of the tricuspid valve, the picture in general being similar to that of the other cases. There were many small pulmonary infarcts, all of which had undergone abscess formation. There was empyema of the right pleural cavity. The spleen was moderately enlarged.

COMMENT

As far as we have been able to determine from the literature and from Dr. Edwin G. Williams of the United States Public Health Service, septicemia due to ordinary organisms must be very uncommon in narcotic addicts. In 4 of the 5 cases reported here the causative organism was Staphylococcus aureus and in one Bacillus pyocyaneus.

None of the patients used any antiseptic precaution in the self administration of the heroin. There are, therefore, several possible modes by which blood stream infection may have occurred. First, the material used may have contained pathogenic bacteria. In general, heroin used by addicts is mixed with various agents for the purpose of adding bulk. One such common adulterant is lactose, which perhaps would improve the mixture as a culture medium. Second, the equipment used in the administration of the heroin was not sterilized and was often passed from one addict to another without cleansing. Third, failure to apply an antiseptic to the skin before injection of heroin intravenously may have permitted the introduction into the blood stream of organisms inhabiting the skin. Fourth, in case 4 the source of the septicemia may have been the abscess which had developed at a site of injection. Presumably, of course, the abscess had its inception by one of the mechanisms previously mentioned. There is no way to determine definitely which of these possible modes of infection operated in these cases. However, the fact that cases 3, 4 and 5 were closely associated chronologically suggests that the heroin was contaminated. On the other hand, patients 3 and 4 were husband and wife, who used a syringe in common.

It is not particularly surprising that acute bacterial endocarditis developed in 4 of these 5 cases of septicemia. However, localization of the lesion on the tri-

cuspid valve alone in 3 of the cases is noteworthy because of its rarity. For example, in a series of 646 cases of acute bacterial endocarditis reported by Goldburgh, Baer and Lieber [4] the tricuspid valve alone was involved in only 20 cases (3.1 per cent). In the remaining case the aortic valve alone was affected. There was no evidence of preexisting valvular disease in any of the cases.

The diagnosis of acute endocarditis was readily apparent in case 1. Manifestations of septicemia, repeatedly positive blood cultures, petechiae and the appearance of an aortic diastolic murmur indicated the existence of bacterial endocarditis of the aortic valve.

In cases of endocarditis involving the right side of the heart the diagnosis may be less apparent. In the 3 cases of this group the presence of septicemia was obvious from the clinical course and the positive blood cultures for Staphylococcus aureus. However, the onset of manifestations of pulmonary infarction indicated the need for discovering a source of the emboli. The absence of any such source in the peripheral veins permitted the deduction that there was right sided endocarditis. The failure to detect a murmur in any case was strong ground for concluding that the tricuspid valve was the seat of the endocarditis. There was no evidence of embolic phenomena in the systemic circulation in any of these cases, and it is interesting that in spite of the presence of staphylococcic septicemia abscesses were found only in the lungs. The diagnostic features of these 3 cases have been discussed in greater detail elsewhere.[5]

The treatment in the 4 cases of endocarditis included the use of average doses of one of the sulfonamides in each case and of penicillin in 1 case. The outcome was uniformly fatal. In case 4, in which there was a large staphylococcic abscess of the antecubital fossa and Staphylococcus aureus septicemia but no endocarditis, incision and drainage of the abscess, sulfamerazine and penicillin successfully controlled the infection.

SUMMARY

In 4 of 5 cases of septicemia in heroin addicts death followed the development of acute bacterial endocarditis, which in 3 instances involved the tricuspid valve alone. Three of the cases of endocarditis were due to Staphylococcus aureus and the fourth to Bacillus pyocyaneus. In the 1 case of Staphylococcus aureus septicemia without endocarditis, recovery occurred.

4. Goldburgh, H. L.; Baer, S., and Lieber, M. M.: Acute Bacterial Endocarditis of the Tricuspid Valve, Am. J. M. Sc. **204**: 319 (Sept.) 1942.

5. Hussey, H. H., and Katz, S.: Septic Pulmonary Infarction, to be published.

Mental Exhaustion from Intellectual Effort.—Bearing on this subject, I, like others of our profession, have had repeated occasion to observe the effect of overwork on gentlemen who use their brains with an expenditure of energy inconceivable to the thoughtless—men of widespread mercantile affairs, men engaged in money transactions on a large and anxious scale. The condition of such patients attested the applicability of these remarks by their mental and physical exhaustion, by their depression of spirits and by their want of self confidence. Yet, with such men, the restoration to health has been made complete by mental leisure, by "going out of town" and taking plenty of exercise in the open air, while abstaining from the real disturbing cause, their business.—Hilton, John: Rest and Pain, London, George Bell & Sons, 1857.

THE TREATMENT OF EARLY AND LATENT SYPHILIS

IN NINE TO TWELVE WEEKS WITH TRIWEEKLY INJECTIONS OF MAPHARSEN

A PRELIMINARY ANALYSIS OF THE RESULTS IN THE FIRST 4,823 CASES

HARRY EAGLE, M.D.

BALTIMORE

The pioneer work of Chargin, Leifer, Hyman and their associates [1] with the five day intravenous drip has stimulated a large number of clinical studies on other intensive methods of antisyphilitic treatment.[2] The duration of treatment has been varied from one day to twenty weeks, the frequency of injections has been varied from twice daily to twice weekly, and in some clinics artificially induced fever has been used as an adjunct to the intensified course of arsenotherapy.

As with any chemotherapeutic procedure, the three major considerations which determine the utility of these treatment schemes are their therapeutic efficacy, their toxicity and their practicability. Recent studies in experimental rabbit syphilis provide a helpful orientation to the first two of these points. The total curative dose of mapharsen was found to be more or less constant, largely independent either of the frequency of injections or of the duration of treatment.[3] On the other hand, the toxicity of the drug varied directly with the method of administration. The shorter the time period over which the mapharsen was administered and the fewer the injections, the greater was its toxicity [4] and the smaller was the margin of safety provided by a given therapeutic dose.[5]

In man also the curative dose of mapharsen has been found to be essentially the same, regardless of the method of administration.[5] From the animal data it was therefore to have been anticipated that, the shorter the time period into which the curative dose of mapharsen was compressed, the greater would be the incidence of serious toxic reactions and death. That has been fully borne out in practice. Thus, weekly injections of 60 mg. of mapharsen represent approximately one tenth the maximal tolerated dose in animals; and, corresponding to that wide margin of safety, the mortality in man following routine weekly treatment at this dosage level has been on the order of 1: 5,000 or less.[6] On the other hand, when the total therapeutic dose of 1,200 mg. of mapharsen was compressed into five days, the calculated margin of safety [5] was only 2.0, and the observed mortality with this schedule in man has been on the order of 1: 200. Between these two extremes, schedules of intermediate degrees of intensity, providing intermediate margins of safety,

Owing to limitations of space, tables 1 and 6 appear in reprints only.

From the U. S. Public Health Service Venereal Disease Research and Postgraduate Training Center, Johns Hopkins Hospital.

Read in a panel discussion on "Intensive Therapy of Early Syphilis, with Special Reference to Arsenotherapy Either Alone or Combined with Other Agents," before the Section on Dermatology and Syphilology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 15, 1944.

1 and 2. Bibliographic titles are given in the reprints.

3. Eagle, H., and Hogan, R. B.: An Experimental Evaluation of Intensive Methods for the Treatment of Early Syphilis: II. Therapeutic Efficacy and Margin of Safety, Ven. Dis. Inform. **24**: 69-79, 1943.

4. Eagle, H., and Hogan, R. B.: An Experimental Evaluation of Intensive Methods for the Treatment of Early Syphilis: I. Toxicity and Excretion, Ven. Dis. Inform. **24**: 33-44, 1943.

5. Eagle, H., and Hogan, R. B.: An Experimental Evaluation of Intensive Methods for the Treatment of Early Syphilis: III. Clinical Implications, Ven. Dis. Inform. **24**: 159-170, 1943.

6. Hahn, R. D.: Antisyphilitic Treatment: Mortality Studies: Clinical, Statistical and Pathologic Analysis of Forty-Seven Fatal Reactions, Am. J. Syph., Gonor. & Ven. Dis. **25**: 659-686, 1941.

necessarily result in a correspondingly intermediate morbidity and mortality (chart 1).

On the basis of the animal data there was reason to believe that a treatment schedule involving injections of mapharsen repeated three times weekly at a unit dose of approximately 1 mg. per kilogram represented a reasonable compromise between speed and safety. This schedule in animals provided a safety factor of 6 to 8.[5] Corresponding to that large margin of safety, it was anticipated that the mortality in man would be less than 1:1,000 and that such a schedule would permit the definitive treatment of early and perhaps of latent syphilis in outpatient clinics within a period of six to twelve weeks. The clinical study was begun in October 1941 with the cooperation of hospital, state, county and municipal venereal disease clinics. The number of participating clinics gradually increased, reaching 86 as of March 1, 1944. These clinics are listed in table 1.

With the exception of those cases treated in Marine hospitals and a few other hospital clinics, all patients were treated as ambulatory outpatients. The dosage was adjusted to body weight, at first with ten different

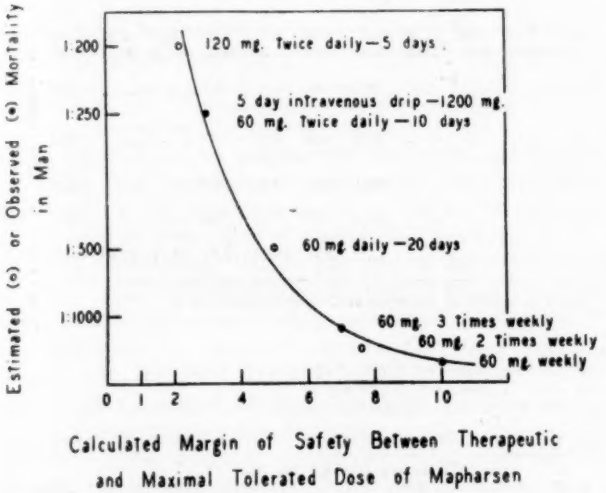
Estimated (o) or Observed (•) Mortality in Man
1:200
1:250
1:500
1:1000
120 mg. Twice daily—5 days
5 day intravenous drip—1200 mg.
60 mg. Twice daily—10 days
60 mg. daily—20 days
60 mg. 3 Times weekly
60 mg. 2 Times weekly
60 mg. weekly
0 1 2 4 6 8 10
Calculated Margin of Safety Between Therapeutic and Maximal Tolerated Dose of Mapharsen

Chart 1.—Mortality of various treatment schedules in man as a function of the margin of safety, calculated from experimental data.

dosage scales, but later with five, as indicated in table 2. The average dose was 60 mg.; the maximum was arbitrarily set at 80 and the minimum at 40 mg. No distinction was made between the sexes. The duration of treatment was varied from four to twelve weeks in order to ascertain the minimum total amount of treatment which would give satisfactory results. In approximately half the clinics the patients were given weekly injections of a bismuth compound concomitant with the arsenical in order to determine the degree to which the end results would be affected by the administration of heavy metal. Although the choice of the bismuth preparation was left to the discretion of the clinic director, 80 per cent of those receiving bismuth were given the bismuth subsalicylate at an average dose of 0.2 Gm., equivalent to 0.13 Gm. of bismuth metal. The clinics were urged to do quantitative rather than qualitative serologic tests in order to permit the detection of serologic relapse in patients not yet seronegative; and it was asked that such tests be repeated at least twice during the period of treatment, and monthly thereafter. It was further requested that a spinal puncture be done three months after the completion of treatment and repeated at the end of a year if feasible.

The present preliminary report is based on the early results in the first 4,823 patients on whom treatment records were submitted for analysis. Although the proportion of patients observed for a year or longer has been small (cf. table 3), it is nevertheless believed that the method of analysis permits preliminary conclusions

TABLE 2.—*Dosage Scale of Mapharsen in Relation to Body Weight of Patients Treated Three Times Weekly*

Weight		Mapharsen, Mg. per Injection
Lbs.	Kg.	
- 90	-40	40
90-120	40-55	50
120-155	55-70	60
155-185	70-85	70
185-	85-	80

TABLE 3.—*Duration of Observation of 3,376 Patients with Primary and Secondary Syphilis*

Weeks after beginning of treatment	<6	6-9	10-14	15-19	20-24	25-29	30-39	40-49	50-59
Patients still under observation.	3,376	2,944	2,249	1,721	1,410	1,154	942	609	388

The progressive falling off is due in part to lapse and in part to the fact that almost half these patients have been treated during the past twelve months.

with respect to therapeutic efficacy in early syphilis and that these conclusions will be modified only slightly as more patients fall into the longer observation periods.

METHOD OF ANALYSIS

As shown in table 4, the 4,823 patients treated included 290 with seronegative primary, 1,054 with seropositive primary, 2,050 with secondary and 1,190

TABLE 4.—*Analysis of 4,823 Cases of Syphilis Treated with Triweekly Injections of Mapharsen*

A. Race, Sex and Age

Race and Sex				Age						
White ♂	Negro ♂	White ♀	Negro ♀	<15	15-17	18-20	21-29	30-44	> 45	Unknown
1,282	1,301	678	1,562	68	523	1,162	2,005	938	106	20

B. Diagnosis [1]

Early Syphilis (3,384)				Latent Syphilis (1,190)			Late Secondary and Treatment Failures (150)		
Primary Seronegative	Primary Seropositive	Total Primary[2]	Secondary[3]	<2 Years' Duration	>2 Years' Duration	Duration Unknown	Reinfection or Recurrent Infectious Relapse	Recurrent Secondary	Serorelapse
290	1,054	1,344	2,050	347	212	631	120	8	31

1. Fifty cases of central nervous system syphilis and 29 with miscellaneous presenting symptoms are not included in the table.
2. 978 dark field positive, 165 dark field negative, 201 dark field not done.
3. Including cases of both primary and secondary syphilis.

C. Amount of Treatment Received

Number of Mapharsen Injections	Number of Patients	Total Mapharsen Mg./Kg.	Without Bismuth	With Bismuth	Total
- 9	384	-14	355	400	755
10-14	367	15-20	201	630	831
15-20	602	21-26	918	1,388	2,306
21-26	2,547	27-	145	606	751
27-	863	?[4]	47	133	180

4. Weight unknown.

with latent syphilis. There were 151 patients previously treated for early syphilis and now diagnosed as presenting infectious relapse or serologic relapse, and 8 with late recurrent syphilis. Forty per cent of the total were white and 53 per cent were male. The amounts of treatment received, expressed both as the number of injections and as the total milligrams per kilogram of body weight, are listed in table 4.

In evaluating the therapeutic results in cases of primary and secondary syphilis, the following types of case were adjudged treatment failures: infectious relapse, clinical evidence of central nervous system involvement, positive Wassermann or flocculation test in the spinal fluid without clinical symptoms, serologic relapse and cases presenting a persistently positive blood test at a more or less stationary level one year after the beginning of treatment. Cases which were strongly suggestive of reinfection rather than relapse were nevertheless considered treatment failures. Cases were adjudged serologic relapse (*a*) if the blood tests reverted to positive after having been negative for a significant period of time, and remained so, or (*b*) if the serum tests, without ever having become negative, showed a definite and continuing upward trend in the quantitative reagin titer. The fact that in only 30 per cent of the cases of early syphilis was a spinal puncture done three months or longer after beginning treatment is not believed to affect the apparent end results materially. Every one of the patients with a positive spinal fluid or clinical evidence of neurosyphilis had a positive serum test. It follows that, of those patients who did not have a spinal puncture, only a negligible proportion adjudged seronegative, clinically well and "cured" would have had a positive fluid.

The methods used in the calculation of the cumulative percentage of treatment failure, and the cumulative percentage of patients becoming and remaining seronegative, are illustrated in table 5.

TOXICITY

The toxic reactions observed in the entire group of 4,823 patients are summarized in table 6, grouped in three categories. The minor subjective reactions of nausea, vomiting, malaise or headache occurred in 16 per cent of the patients, and approximately 1.5 times more often in women than in men. The incidence of these reactions differed widely among individual clinics, and psychologic factors as well as the varying quality of medical care undoubtedly contributed to that varying frequency. In 23 patients, or 1 in every 210 treated, the repetition and severity of these ordinarily minor complaints made it necessary to discontinue treatment.

In 106 of the patients a syndrome was observed suggestive of sensitization to mapharsen and resembling that observed in some patients receiving a sulfonamide compound. The symptoms varied from patient to

TABLE 5.—*Method Used in the Calculation of the Cumulative Percentage of Treatment Failure and "Cure"*

(Patients with primary and secondary syphilis who received 21 mg./Kg. mapharsen or more, with concomitant injections of bismuth)

	Weeks after beginning of treatment	-6	6-7	8-9	10-11	12-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-59[1]	60-69[1]
(1)	No. patients under observation	1,341	1,338	1,300	1,079	913	789	623	505	375	291	215	160	121	55
(2)	No. treatment failures observed at indicated time	.....	.....	.....	.....	.....	1	3	2	1	5	.....	1	5	1
(3)	Apparent per cent failing	.....	.....	.....	.....	.....	0.13	0.48	0.4	0.27	1.72	.....	0.63	4.13	1.82
(4) = 100 — (3)	Apparent per cent not failing	100	.....	.....	.....	.....	99.87	99.52	99.6	99.73	98.28	100	99.37	95.87	98.18
(5) from (4)	Cumulative per cent not failing	.....	.....	.....	.....	.....	99.87	99.39	98.99	98.72	97.02	97.02	96.41	92.43	90.75
(6) = 100 — (5)	Cumulative per cent treatment failure	.....	.....	.....	.....	.....	**0.13**	**0.61**	**1.01**	**1.28**	**2.98**	**2.98**	**3.59**	**7.57**	**9.25**
(7)	No. becoming seronegative	144	63	78	76	99	113	61	27	25	9	6	4	5	1
(8) = (7) × 100 / (1)	Apparent per cent becoming seronegative	10.73	4.7	6.0	7.04	10.85	14.32	9.90	5.42	6.67	3.09	2.79	2.50	4.13	1.82
(9) = (8) × (5)	Per cent becoming seronegative, corrected for those already failed	10.73	4.7	6.0	7.04	10.85	14.32	9.89	5.39	6.6	3.05	2.71	2.43	3.98	1.67
(10) from (9)	Cumulative per cent becoming seronegative	10.73	15.43	21.43	28.47	39.32	53.64	63.53	68.92	75.52	78.57	81.28	83.71	87.69	89.36
(11)	No. patients, once seronegative, developing treatment failure	.....	.....	.....	.....	.....	.....	2	2	1	5	.....	.....	3	1
(12) = (11) × 100 / (1)	Apparent per cent above failures, referred to total patients under observation (1) as 100	.....	.....	.....	.....	.....	.....	0.32	0.40	0.27	1.72	.....	.....	2.48	1.82
(13) = (12) × (5)	Corrected per cent above failures, referred to total patients under observation (1) as 100	.....	.....	.....	.....	.....	.....	0.32	0.4	0.27	1.67	.....	.....	2.31	1.64
(14) from (13)	Cumulative per cent of total population who failed after once being seronegative	.....	.....	.....	.....	.....	.....	.....	0.72	0.99	2.66	.....	.....	4.97	6.61
(15) = (10) — (14)	Cumulative per cent becoming and remaining seronegative	.....	.....	.....	.....	.....	.....	.....	**6.82**	**74.53**	**75.91**	**78.72**	**81.05**	**82.72**	**82.75**

1. Figures in these columns of dubious quantitative significance because of small numbers of patients still under observation.

TABLE 7.—*Effect of Amount of Mapharsen Treatment (Total Mg./Kg.) on Number of Treatment Failures in 3,376 Cases of Primary and Secondary Syphilis*

		Patients Receiving Mapharsen Alone					Patients Receiving Bismuth Plus Mapharsen				
		Total Mapharsen Dosage, Mg./Kg.									
	Total	<15	15-20	21-26	27-	Total	<15	15-20	21-26	27-	Total
Number of patients treated	3,376	297	134	568	94	1,135	327	473	908	423	2,241
Mean period of observation (weeks)	24	21	24	33	28	28	7	22	23	26	21
Reinfection or relapse	87	19	6	31	3	61	3	14	6	3	26
Serorelapse	81	8	3	45	6	62	1	11	3	2	19
Clinical neurorecurrence	12	5	1	4	..	10	..	1	1	..	2
Spinal fluid positive (asymptomatic)	14	5	..	2	..	7	..	4	3	..	7
Seroresistance	14	7	2	2	..	12	..	1	1	..	2
Total treatment failures	208	44	12	84	9	152	4	31	14	5	56
Apparent incidence of failure,[2] %	6.2	14.8	9.0	14.8	9.6	13.4	..	6.6	1.5	1.1	2.5
Comment		In patients not receiving bismuth there was a uniformly high incidence of treatment failure					In patients receiving bismuth there were fewer treatment failures, and in proportion to the total amount of treatment received				
		Even large amounts of mapharsen alone were not as effective as moderate amounts of mapharsen supplemented by 5 to 8 injections of bismuth									

1. Eighty per cent of patients receiving bismuth were given the subsalicylate, once weekly, in average dose of 0.2 Gm. (0.13 Gm. of bismuth metal). Total number of bismuth injections was approximately one third of the total mapharsen dosage in milligrams per kilogram. For the corrected cumulative percentage of treatment failures and "cures" in relation to the method of treatment, compare charts 1, 2 and 3.

2. These figures are of relative and not of absolute significance, since they refer the failures to the original number of patients treated and do not take into consideration the fact that the number of patients under observation fell off steadily after treatment was completed.

patient and occurred in varying combination. In order of decreasing frequency they consisted of fever, rash, vomiting, headache, conjunctivitis and photophobia, and facial edema. Most of these patients recovered completely in forty-eight to seventy-two hours. In 24 of 62 patients tested in that respect soon after recovery,

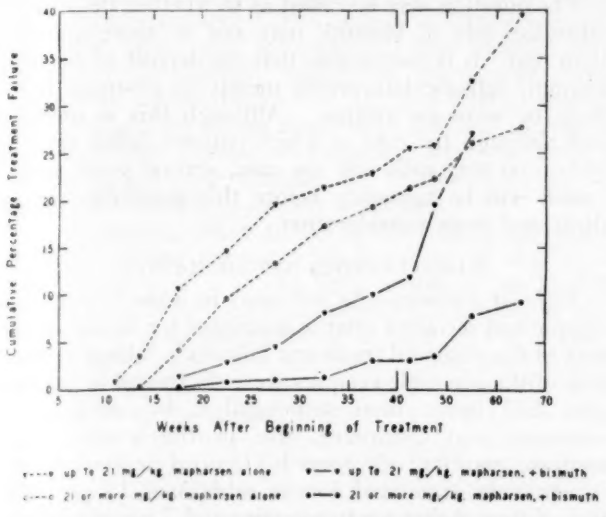
Cumulative Percentage Treatment Failure
Weeks After Beginning of Treatment
up to 21 mg./kg. mapharsen alone
21 or more mg./kg. mapharsen alone
up to 21 mg./kg. mapharsen, + bismuth
21 or more mg./kg. mapharsen, + bismuth

Chart 2.—Cumulative percentage of treatment failure in patients treated triweekly, in relation to the total dose of mapharsen and bismuth.

actual sensitization to mapharsen was demonstrated in that small doses precipitated the same syndrome; and in a total of 54 patients, or 1 in every 90 patients treated, it was necessary to discontinue arsenical treatment. It is of interest that 70 per cent of these reactions occurred in the second to fourth week of treatment and 60 per cent in the second week; between the eighth and the fourteenth day of treatment. The time period, coupled with the high frequency of an associated toxic rash, suggests a close relationship of this syndrome to so-called erythema of the ninth day.

Serious toxic reactions occurred in a total of 39 patients. They consisted of 2 cases of toxic encephalopathy (1:2,400), 7 cases of arsenical dermatitis (1:700), 4 of nephritis (1:1,200), 5 of blood dyscrasia (1:950) and, as the most frequent complication, 21 cases of jaundice (1:250). As with the "sensitization syndrome," 40 per cent of these serious reactions occurred in the second week of treatment and 75 per cent in the second to the fourth week. In general, toxic reactions occurred most frequently during the second week of treatment; beyond that period there was progressively decreasing likelihood of a serious toxic complication.

There were four deaths in the entire series of 4,823 patients: 2 cases of nephritis, 1 of toxic encephalopathy and 1 of jaundice, all occurring in the second to fourth week of treatment. This mortality of 1:1,200 is reasonably close to that anticipated on the basis of animal data but should be further qualified in that two, and perhaps three, of these deaths may have been preventable. With reasonably good medical care the mortality on the triweekly schedule may therefore be 1:2,000 or less rather than 1:1,200.

Unlike the mild reactions to mapharsen, and unlike the syndrome suggestive of sensitization to mapharsen, serious toxic reactions tended to occur in women, in young patients and in Negroes. Thus, all four deaths were in Negro women, 3 of whom were under 18. This tendency for serious reactions to occur in women is of particular interest in relation to the treatment of syphilis in the armed forces. In the 2,583 men represented in the present study no deaths occurred, there were 14 serious reactions, including 11 cases of jaundice, and treatment had to be discontinued for any reason in a total of only 48.

THERAPEUTIC RESULTS IN EARLY SYPHILIS

When the mapharsen was given alone, without bismuth, the results were uniformly poor, regardless of the amount of arsenical administered. The number of observed failures per hundred patients treated differed but little in patients receiving a total of less than 15, 15 to 20, 21 to 26 or 27 or more mg. of mapharsen per kilogram (15, 9, 15 and 10 per cent treatment failures respectively, cf. table 7). However, when bismuth was given along with the mapharsen the results were consistently better, and the optimum results far exceeded those it was possible to attain with mapharsen alone. In patients receiving a total of 15 to 20, 21 to 26 and 27 or more mg. of mapharsen per kilogram plus an average of six, eight and ten injections of bismuth respectively, the incidence of observed treatment failures was 6.6, 1.5 and 1.1 per cent respectively.

These figures are of relative rather than absolute significance because of the large proportion of patients who disappeared from observation. A statistically more reliable comparison is afforded by the cumulative percentage of treatment failure and the cumulative percentage of "cure" calculated by the method illustrated in table 5. The results are in complete agreement with those obtained by the crude method of analysis that has been outlined. As shown in charts 2 and 3, mapharsen alone (the open circles and triangles in charts 2 and 3) gave uniformly poor results.

The addition of an average of only five injections of bismuth to the smaller amount of mapharsen (less than

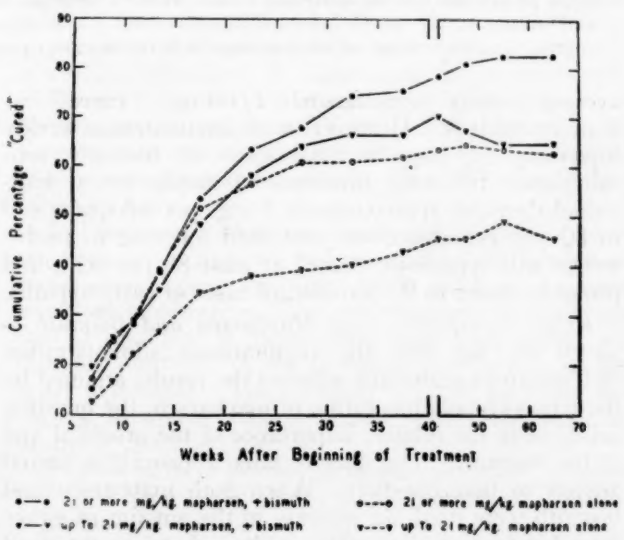
Cumulative Percentage "Cured"
Weeks After Beginning of Treatment
21 or more mg./kg. mapharsen, + bismuth
up to 21 mg./kg. mapharsen, + bismuth
21 or more mg./kg. mapharsen alone
up to 21 mg./kg. mapharsen alone

Chart 3.—Cumulative percentage of "cure" in patients treated triweekly, in relation to the total dose of mapharsen and bismuth.

21 mg. per kilogram) significantly decreased the percentage of definite failure and increased the percentage of "cure" in fifty to sixty weeks from 49 to 65. When an average of nine injections of bismuth was added to the larger amount of mapharsen (21 mg. per kilogram or more) the cumulative percentage of treatment failure seventy weeks after beginning treatment fell to 9.3, and

82 per cent of the patients were seronegative and "cured," with the remainder of the cases still pending (closed circles in charts 2 and 3).

In summary, at least in the triweekly schedule, and perhaps in other intensified forms of arsenotherapy as well, mapharsen should be supplemented by bismuth for optimum results. In the absence of heavy metal a relatively small amount of mapharsen (up to 20 mg. per kilogram, averaging a total of 800 mg.) "cured" half of the patients, and even twice that amount, an average total of approximately 1,600 mg., "cured" less than two thirds. However, with simultaneous weekly injections of bismuth (0.2 Gm. of bismuth subsalicylate), triweekly injections of mapharsen at individual doses of approximately 1 mg. per kilogram (40 to 80 mg. per injection) continued for nine to twelve weeks will apparently "cure" at least 80 per cent, and probably closer to 90 per cent, of cases of early syphilis.

TABLE 8.—*Incidence of Observed Treatment Failures*[1] *in Relation to Amounts of Bismuth and Mapharsen Received*

Total Mapharsen, Mg./Kg.	Incidence (%) of Treatment Failure in Patients Receiving Indicated Number of Bismuth Injections: None (796)	1-4 (53)	5-8 (881)	9 and over (879)
15-20	9[1]	..[2]	7.3	2.6
21-26	15	..	1.8	1.3
27 and over	9.6	..	...	1.1
Total	13.2	8±	4.0	1.4

1. Although the actual cumulative percentage of treatment failure was several times the apparent incidence as listed above, these figures do reflect the relative efficacy of the various treatment schedules.
2. Results not significant because of small number of patients.

Relative Importance of Mapharsen and Bismuth.—Given the fact that the simultaneous administration of bismuth so materially affected the results attained by the triweekly administration of mapharsen, the question arises as to the relative importance of the arsenical and of the bismuth. The data of table 7 provide a partial answer to that question. When both mapharsen and bismuth were used, an increase in the amount of either drug led to more favorable results. A relatively small amount of mapharsen (15 to 20 mg. per kilogram) supplemented by nine injections or more of bismuth gave results comparable to those achieved by larger amounts of mapharsen with smaller amounts of bismuth. In that sense the drugs were mutually supplementary. However, even the largest amount of mapharsen alone (27 or more mg. per kilogram, averaging 30) was less effective than relatively small amounts of mapharsen and bismuth used in conjunction (15 to 20 mg. of mapharsen per kilogram plus approximately six injections of bismuth). The two drugs are apparently not merely additive but actually synergistic in their therapeutic effects. This suggests that they may exert their spirocheticidal action by affecting different vital functions of the organism.

The question may be raised as to whether the striking adjuvant role of bismuth may not be more apparent than real. It is conceivable that the deposit of insoluble bismuth subsalicylate serves merely to postpone infectious or serologic relapse. Although this is unlikely, and although the rate at which patients failed gave no indication that such was the case, several years' observation will be necessary before this possibility can be dismissed from consideration.

MISCELLANEOUS CONSIDERATIONS

Type of Failure.—As indicated in table 6, infectious relapse and serologic relapse accounted for 43 and 40 per cent of the observed treatment failures. A large proportion of the serologic relapses were diagnosed in patients who had never been seronegative, by virtue of a sustained and continuing rise in the serum reagin content, quantitatively titered. Central nervous system involvement accounted for an additional 13 per cent, half of these being asymptomatic; and 7 per cent of the failures were of patients whose serologic findings were positive at a stationary level one year after the beginning of treatment. The degree to which the central nervous system failures represented cases of central nervous system involvement at the time treatment was begun is an open question.

TABLE 9.—*Analysis of Treatment Failures in 908 Cases of Primary and Secondary Syphilis Treated with a Total of 21-26 Mg. of Mapharsen per Kilogram and Concurrent Injections of Bismuth*

	Totals	Race and Sex: White ♂	Negro ♂	White ♀	Negro ♀	Initial Serologic Titer[1]: 0	1-7	8-31	32-	Diagnosis: Seroneg. Primary	Seropos. Primary	Secondary	Duration of Treatment, Days: -68	58-76	77-
Number of patients	908	244	244	99	321	75	76	131	248	75	282	551	335	315	258
Mean period of observation, weeks	23	16	24	28	25	..	..	..	..	..	..	..	..	..	..
Number of treatment failures, all types	14	6	3	2	3	1	2	1	3	1	2	11	5	6	3
Apparent incidence treatment failures	1.6	2.4	1.2	2.0	1.0	1.3	2.6	0.8	1.2	1.3	0.7	2.0	1.5	1.9	1.2

Comment: No demonstrable correlation between the incidence of observed treatment failure and either race, sex, initial serologic titer or the duration of treatment. As in the entire series, fewer failures were observed in seropositive primary syphilis than in secondary syphilis. There was certainly no evidence that the latter has a more favorable prognosis because of a putative immunity.

1. Titer = highest dilution of serum giving a definitely positive result.

Outcome as Influenced by Stage of Infection.—On the basis of previous studies, the prognosis of early syphilis is generally considered better in secondary syphilis than in the seropositive primary stage.[7] In explanation it is usually assumed that the patient with secondary syphilis has had time to develop a certain degree of immunity. However, the present study gave no indication of a more favorable prognosis in secondary syphilis.

Relapsing and Recurrent Syphilis.—In patients with previously treated early syphilis who had relapsed, the number of treatment failures significantly exceeded those obtained in previously untreated syphilis, but only when mapharsen was given alone, without bismuth. In those patients who received mapharsen plus bismuth, the prognosis was apparently no less favorable than in previously untreated cases. However, the number of

7. Moore, J. E.: The Modern Treatment of Syphilis, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1941, pp. 581-588.

patients was small, and further experience and observation may alter the picture unfavorably (table 10).

Rate of Serologic Reversal.—Although, as shown in table 9, the initial serologic titer had no effect on the prognosis of early syphilis, it did materially affect the time required for serologic reversal. As is shown in chart 4, in a group of patients who received similar amounts of treatment (21 to 26 mg. of mapharsen, plus bismuth), those with a low reagin titer attained seronegativity considerably faster, on the average, than those with initially high titers. It is of interest that the rate at which the serum reagin titer fell, and the rate at which patients became seronegative, were the same in this semi-intensive schedule of treatment as in the traditional method of weekly injections.

The question comes up as to the relative efficacy of treatment when the same total dosage of mapharsen was spread over a longer time period, either because treatment was irregular or because the individual dose was smaller than that indicated in table 2. On the basis of the animal data [3] one would have anticipated little or no difference in the end results; and that has been the experience in the present study. As shown in the last section of table 9, in patients receiving similar total amounts of treatment (21 to 26 mg. of mapharsen per kilogram), all of whom also received bismuth, there was no significant difference in the number of observed failures if treatment was completed in less than fifty-eight days (averaging fifty-four), in fifty-eight to seventy-seven days (averaging sixty-six) or in more than seventy-seven days (averaging eighty-one). Within these limits, occasional lapses in treatment or the use of e. g. a biweekly instead of a triweekly schedule had no effect on therapeutic efficacy. The important consideration was the total amount of drug received rather than the intensity or regularity of its administration.

Latent Syphilis.—In 945 of the 1,190 cases of latent syphilis included in the present study, no previous treatment had been given and they were diagnosed on serologic grounds alone. In 279 of these the disease was believed to be of less than two years' duration. In this presumably most favorable group, 99 were given the schedule of treatment found to be most effective in early syphilis (more than 21 or more mg. of mapharsen per kilogram, with simultaneous weekly injections of bismuth). Of these only 25 had become seronegative during a varying period of observation. This is consistent with the results obtained with routine standard methods of treatment.[8] However, since the goal of treatment in latent syphilis is not seronegativity but rather permanent freedom from symptoms, and since a relatively small amount of standard weekly treatment apparently suffices for that purpose,[8] there is every reason to anticipate that an intensive schedule of treatment which is adequate for early syphilis will be equally satisfactory for the treatment of latent syphilis. Because of the generally favorable prognosis of latent syphilis, even with little or no treatment, many years' observation of a large group of patients will be necessary to establish this point.

TABLE 10.—*The Relative Incidence of Treatment Failure in Relapsing or Recurrent Syphilis, Compared with Previously Untreated Early Syphilis*

	Primary and Secondary Syphilis		Infectious Relapse, Serologic Relapse and Recurrent Syphilis	
	Without Bismuth	With Bismuth	Without Bismuth	With Bismuth
Number of patients	1,135	2,241	89	70
Average period of observation	28	21	33	26
Number of failures	152	56	21	2
Incidence of apparent failure, %	13.4	2.5	23.6	2.8

Comment: In patients who received only mapharsen, the relapsing group gave significantly more failures; in patients who received bismuth as well as mapharsen there was no significant difference in the prognosis of recurrent or relapsing syphilis and previously untreated cases of early syphilis.

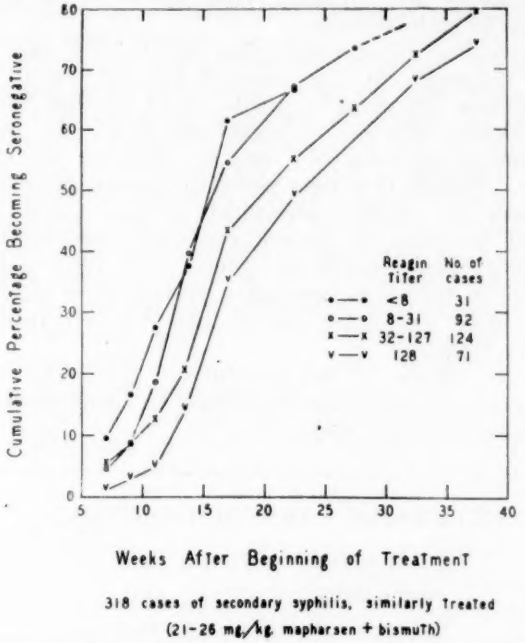

Chart 4.—Rate at which patients became seronegative, in relation to the initial serum reagin titer.

SUMMARY

1. A total of 4,823 patients, including 3,394 cases of primary and secondary, 1,190 of latent and 159 of recurrent or relapsing syphilis, have been treated with triweekly injections of mapharsen at approximately 1 mg. per kilogram per injection, with a maximum of 80 mg. and a minimum of 40. Two thirds of the patients were given concomitant weekly injections of a bismuth compound, usually bismuth subsalicylate (0.2 Gm.).

2. Treatment had to be interrupted because of toxic reactions in a total of 106 patients. Thirty-nine of these were serious reactions, with jaundice the most common complication. Four patients died. It is believed that at least two of these deaths were preventable and that the mortality of the triweekly schedule is on the order of 1:2,000. The incidence of toxic reactions was highest in young Negro women, and there were no deaths in the 2,583 men.

3. Triweekly injections of mapharsen alone, without bismuth, gave uniformly poor therapeutic results, regardless of dosage.

4. Triweekly injections of mapharsen in conjunction with weekly injections of bismuth proved highly effective. In patients receiving an average total of 1,600 mg. (21 mg. per kilogram or more) plus an average total of nine injections of bismuth, the cumulative percentage of treatment failure was 9.3 and the cumulative percentage of "cure" fifty to sixty weeks after the beginning of treatment was 82 per cent. A decrease in either mapharsen or bismuth to less than these amounts resulted in a higher proportion of treatment failure.

8. Diseker, T. H.; Clark, E. G., and Moore, J. E.: Long-Term Results in the Treatment of Latent Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **28**: 1-26, 1944.

5. Although these results are tentative, based on the prolonged observation of as yet a small proportion of the total patients treated, it is believed that triweekly injections of mapharsen at approximately 1 mg. per kilogram, combined with weekly injections of 0.2 Gm. of bismuth subsalicylate and continued for nine to twelve weeks, will probably "cure" 85 to 90 per cent of cases of early syphilis.

6. (*a*) The initial reagin titer affected the rate at which seronegativity was obtained but did not affect the ultimate percentage "cured." (*b*) Within fairly wide limits (fifty-four to eighty-one days) the total duration of treatment also had no effect on the end results. Within that time period occasional lapses in treatment or smaller individual dosages could be ignored, provided the patient eventually received the scheduled total amount of drug. (*c*) With equal amounts of treatment, secondary syphilis gave significantly more treatment failures than did seropositive primary syphilis.

7. The efficacy of this schedule in the prevention of congenital syphilis, and its efficacy in latent syphilis, are under continued study.

INTENSIVE ARSENOTHERAPY

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JEROME K. FISHER, M.D.
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We are presenting a report of 332 cases of early syphilis treated in the past three years with massive doses of arsphenamine by the syringe method, the treatment period being five to six days. Arsphenamine [1] was chosen because of our experience in the rapid healing of syphilitic lesions and the spectacular cures we had witnessed with this drug in early syphilis when other arsenicals had failed, and again because of the excellent results we had obtained in the treatment of early syphilis at the Vanderbilt Clinic over a period of some twelve years with this arsenical. Such observations encouraged us to think that some one should evaluate this drug in an intensive treatment program of early syphilis, i. e. the five day treatment.

We were prompted to undertake this study by the encouraging results of Leifer, Chargin and Hyman,[2] who treated 382 patients by the intravenous drip method with neoarsphenamine and mapharsen. They reported a completely satisfactory course in 81 per cent of their cases. Further study was carried on by various investigators under this plan or modification of Chargin's technic. Rattner [3] used mapharsen by the intravenous drip method in his series. Schoch and Alexander [4] used mapharsen by the syringe method daily over periods of two to four weeks. Of 103 patients they followed for six to eighteen months, 77 per cent are in a satisfactory condition. Shaffer [5] used mapharsen in his series of 430 patients. Cole,[6] including the results of his own work, has summarized the studies of these and other investigators, including a discussion of some work done by Dr. Rattner subsequent to that mentioned and not reported elsewhere.

SELECTION AND CARE OF PATIENTS

All patients treated were men between the ages of 15 and 64 years, chiefly young, healthy men. One patient had active pulmonary tuberculosis, several had hypertension, 1 had a history of jaundice and a number had various skin eruptions other than syphilitic. Several were obese, and a few were thin and emaciated. All these seemingly defective patients were considered poor risks, but they tolerated the treatment as well, apparently, as the otherwise healthy individuals. Two thirds were Negroes. Most of the cases were supplied by the board of health.

All patients were hospitalized for treatment. The ward was under constant nursing care day and night, and a team of physicians gave the treatments, made all tests and closely observed each patient while in the hospital. The injections were given at three to four hour intervals during the daytime.

Every patient had a complete history and physical examination on admission. Two hundred and ninety-six had positive dark fields, and these dark field examinations were repeated daily until they were negative. Sixty-one cases were seronegative. Titrated blood Wassermann reactions were done on patients entering the ward and before discharge. Only 19 were found to have positive spinal fluid Wassermann reactions. These spinal fluid examinations were repeated at the completion of treatment. The blood and platelet counts were within normal limits. These counts were repeated after completion of the course of treatment. Albuminuria was present in 7 cases on admission. Urinalyses were done daily on all patients during the time of treatment. Eighty-nine cephalin flocculation reactions were slightly to strongly positive on admission and became negative in one week to several months following discharge from the hospital. Dr. Franklin Hanger,[7] who has made a study of postarsphenamine liver damage and in whose laboratory the latter tests were done, stated (in a personal communication) that these positive reactions before treatment possibly signified liver damage from syphilis. The serum bilirubin and the blood urea nitrogen were found to be within normal limits on admission. These and the cephalin flocculation reactions were repeated when indicated. Frei and Ducrey tests and urethral cultures were done on all patients. Fifty-nine patients were found to have a slightly to a strongly positive Frei test when read at forty-eight hours. Sixty-nine had a

The beds in the ward were lent by the Department of Medicine.
Dr. Franklin M. Hanger, associate professor of medicine, did all of the functional liver tests.
From the Department of Dermatology, Columbia University College of Physicians and Surgeons, and the Presbyterian Hospital.
Dr. Walter W. Palmer, professor of medicine, and Dr. J. Gardner Hopkins, professor of dermatology, served in an advisory capacity.
Read in a panel discussion on "Intensive Therapy of Early Syphilis, with Special Reference to Arsenotherapy Either Alone or Combined with Other Agents," before the Section on Dermatology and Syphilology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 15, 1944.

1. Cannon, A. B.: Optimal Treatment for Early Syphilis Based on a Twenty Year Trial of Arsphenamine, Bismuth and Mercury Preparations, Am. J. Syph., Gonor. & Ven. Dis. **21:** 155, 1937.
2. Leifer, W.; Chargin, L., and Hyman, H. T.: Massive Dose Arsenotherapy of Early Syphilis by Intravenous Drip Method, J. A. M. A. **117:** 1154 (Oct. 4) 1941.
3. Rattner, H.: Five Day Treatment of Syphilis, Illinois M. J. **81:** 29, 1942.
4. Schoch, A. G., and Alexander, L. J.: Short Term Intensive Arsenotherapy of Early Syphilis: Preliminary Report, Am. J. Syph., Gonor. & Ven. Dis. **25:** 607, 1941; Intensive Arsenotherapy of Early Syphilis: Follow-Up Report on the Ten Day Syringe Method of Treatment, Arch. Dermat. & Syph. **46:** 128 (July) 1942.
5. Shaffer, L. W., and Salchow, P. T.: Report of Social Hygiene Division, Detroit Department of Health, September 1942.
6. Cole, H. N.; Heisel, E. B., and Stroud, G., III: Intensive Methods of Treating Syphilis, J. A. M. A. **123:** 253 (Oct. 2) 1943.
7. Hanger, F. M., Jr., and Gutman, A. B.: Postarsphenamine Jaundice, J. A. M. A. **115:** 263 (July 27) 1940.

slightly to a strongly positive Ducrey skin test at forty-eight hours, and 21 had positive urethral cultures for gonorrheal organisms. No evidence of syphilitic involvement was found on x-ray examination of the heart or aorta. Electrocardiograms were done on the first half of the series. No noteworthy abnormalities were discovered. Rectal temperature, pulse rate and respiration were recorded on each patient every four hours.

A record was kept of the time required for spirochetes to disappear from surface lesions, of the healing of lesions, of the disappearance of glands and of all reactions to treatment.

After discharge from the hospital the patients were followed weekly in the clinic, where physical examinations and titrated blood Wassermann reactions were done. After the initial period of six weeks the patients were followed monthly.

TREATMENT PLAN

Our procedure consisted in giving arsphenamine in 2 per cent solution by the syringe method three to four times daily for five to six days, depending on the particular variation of our plan. The total dosage ranged from 1.5 Gm. in the beginning of the experiment to 4.4 Gm. in the latter part of the treatment program. As arsphenamine had never been used in the five day treatment program, we began cautiously with small doses. Experience showed that the reactions were chiefly of a mild sort, so we increased the number of injections from three to four times a day, and the number of days from five to six.

VARIATIONS OF TREATMENT PLAN

We employed seven different treatment plans (table 1), each new plan having been worked out after a study of the results of the preceding one. The dosage was gaged according to the weight of the patient, each group being divided into light weight (100 to 135 pounds or 45 to 61 Kg.), medium weight (135 to 165 pounds, or 61 to 75 Kg.) and heavy weight (165 to 220 pounds, or 75 to 98 Kg.), so that the light weight received a total of 1.5 Gm., the middle weight 2.1 Gm. and the heavy weight 2.85 Gm. of arsphenamine, given three times a day for five days. The dose was increased each day.

Forty-seven patients were treated under this plan. At the end of the first day's treatment, 52.5 per cent of the patients had negative dark fields. Two required four days before their dark fields became negative. Mucocutaneous relapses with positive dark fields began to appear. It quickly became evident that this plan had proved a failure. The reactions had been of an exceedingly mild type except for an encephalitis in the forty-seventh patient, so it was decided that the amount of arsenic could be increased. In order to do this the treatment was extended to six days instead of five, with a corresponding increase in the amount of arsphenamine in each weight group.

Plan Variation 2.—This increase gave the light weights a total of 1.8 Gm., the middle weights 2.55 Gm. and the heavy weights 3.45 Gm.

Forty cases were treated in this group. Sixty per cent had negative dark fields after one day's treatment, 83 per cent were negative after the second day and 95 per cent were negative after the third day. One patient was dark field positive for as long as five days. The reactions remained mild, except for the second case of encephalitis, the fifth patient treated under this new scheme. It soon became evident that some radical change must be made in the treatment program in order to hasten the disappearance of spirochetes from the lesions and to prevent mucocutaneous relapses.

Plan Variation 3.—The first radical departure from the original treatment program was to give the largest doses on the first day and gradually diminish the amount toward the end of the treatment. We gave the injections four times a day and increased the amount of arsphenamine to 2.0 Gm. for the light weights, 2.6 Gm. for the middle weights and 3.45 Gm. for the heavy weights. We were prompted to begin the treatment with large doses on the first day because of the lack of serious reactions and of the patient's good general condition at this period of treatment. Furthermore, we were convinced that the greater the initial dosage in the first day or two of treatment the more favorable would be the result. Large doses in the beginning had the added advantage that, should the treatment have to be discontinued because of reactions, the patient would already have received a substantial part of his treatment in the first two days, virtually half the total amount of arsphenamine planned for the course.

Of the 60 patients treated under this third plan, 96 per cent were negative on dark field examination after the first day of treatment and 100 per cent were negative at the end of the second day, a decided improvement over the other two plans. The serologic responses were most encouraging, a number of patients becoming negative and others showing pronounced reduction in the intensity of the reactions. While frequency and intensity of all the reactions were somewhat increased, especially the initial rise in temperature, they were not serious. Even though the individual had a Herxheimer reaction with a temperature of 104.2 F., the injection of arsphenamine was given. The next morning the patient's temperature would be normal and he would be none the worse.

TABLE 1.—*Plan Variations in the Treatment with Arsphenamine*

Plan Variation	Number of Cases Treated	Number of Days Treated	Number of Injections per Day	Total Amount Arsphenamine Given 1st Day (Gm.)	Total Amount Arsphenamine Given Last Day (Gm.)	Total Amount Arsphenamine Given in the Course: Light Weight 100 Lb. to 135 Lb. (Gm.)	Medium Weight 135 Lb. to 165 Lb. (Gm.)	Heavy Weight 165 Lb. to 220 Lb. (Gm.)
1	47	5	3	0.3 to 0.45	0.3 to 0.6	1.5	2.1	2.85
2	40	6	3	0.3 to 0.45	0.3 to 0.6	1.8	2.55	3.45
3	60	6	4	0.45 to 1.0	0.2 to 0.3	2.0	2.60	3.45
4	103	6	4	0.6 to 1.0	0.4	3.0	3.0	3.6
5*	27	3*	4*	1.0	1.0	...	3.0	...
6	18	6	4	1.0	0.4	3.4	4.0	4.4
7	37	6	4	1.0	0.4	3.2	3.6	4.0

* Plan 5 consisted in giving 1.0 Gm. of arsphenamine in four divided doses a day on three alternate days.

After six months infectious relapses began to make their appearance. A study was then made of all cases treated to date in each variation of our plan of treatment, and it was observed that no patient who had received as much as 3.0 Gm. of arsphenamine had suffered a relapse. It appeared that if each patient could be given a minimum of 3.0 Gm. that might be the answer to our problem.

Plan Variation 4.—This was devised whereby the light weight and middle weight groups each received 3.0 Gm., and the heavy weight group 3.6 Gm. One hundred and three patients were treated in this plan. All except 1 had a negative dark field after the first day of treatment. While the incidence of initial febrile reactions remained about the same as in the previous group treated under plan 3, there was a 6 per cent increase in toxic erythema. Optimism over this plan of treatment was soon dispelled by the appearance of mucocutaneous relapses in spite of the minimum 3.0 Gm. dose that had been given.

TABLE 2.—*Time Required for Dark Fields to Become Negative*

Plan Variation	Dark Field Positive Cases	Negative After 1st Day, per Cent	Negative After 2d Day, per Cent	Negative After 3d Day, per Cent	Negative After 4th Day, per Cent	Negative After 5th Day, per Cent
1	40	52.5	90.0	95.0	100.0	
2	38	60.5	83.7	95.2	97.9	100.0
3	50	94.0	100.0			
4	86	98.9	100.0			
5	27	100.0				
6	18	100.0				
7	37	100.0				

TABLE 3.—*Outcome of Treatment*

Number of cases	332
Observed 6 months to 3 years	178
Observed 9 to 11 months, outcome pending (2%)	3
Clinically and serologically negative (66%)	118
Unsatisfactory outcome (32%)	57
Cutaneous relapses with positive dark field	36
(Negative blood Wassermann before cutaneous relapse—24)	
Serorelapse after becoming seronegative	9
Did not become serologically negative in 12 months	12
Failed to become serologically negative sometime during observation regardless of outcome	27

Plan Variation 5.—Examination of the blood arsenic reports done in the cases showed a sharp rise in the arsenic level on the second day and a tendency toward a more gradual rise on the last days of the treatment. By giving 1.0 Gm. in four divided doses every other day for a total of 3.0 Gm. in five days, we thought that the intervening day of rest would allow for the excretion of sufficient amounts of arsenic to maintain the blood arsenic at a more even level. All 27 patients treated under this plan were middle weights. All dark fields were negative at the end of the first day's treatment and there was a very satisfactory serologic response, but even though we have followed only 13 patients for six months we have had 3 mucocutaneous relapses. There was an increase both in initial rise in temperature of 16 per cent of the patients and in secondary rise in temperature of 10 per cent.

Plan Variation 6.—Although it was apparent from the increased number of reactions that we were approaching the highest total amount of arsenic that an individual could tolerate in six days, we decided to make an increase in the amount of arsphenamine to 1.0 Gm. the first day for each patient and gradually reduce the dose toward the end of treatment. In this plan the light weights received a total of 3.4 Gm., the middle weights 4.0 Gm. and the heavy weights 4.4 Gm. in six days. Eighteen patients were treated according to this outline. All dark fields were negative by the completion of one day's treatment. Of the 8 patients that we have followed for at least six months, no relapses have occurred. This group has given the best clinical and serologic results of any so far treated, but at a cost of great increase in reactions. Toxic erythemas occurred in 55.5 per cent of the patients, secondary fevers in 89 per cent and toxic neuritis in 39 per cent. Although not severe, these reactions have been so frequent as to cause us to make a reduction in the dosage.

Plan Variation 7.—The last plan variation, 7, called for 1.0 Gm. of arsphenamine the first day in all groups of patients. For the light weight group we gave a total of 3.2 Gm., the middle weight group 3.6 Gm. and the heavy weight group 4.0 Gm. Thirty-seven patients were treated in this group. All dark fields were negative by the end of the first twenty-four hours of treatment. Although only 2 patients in this group were followed for six months, 1 had a mucocutaneous relapse on the eighty-first day after completion of the treatment.

OUTCOME OF TREATMENT

The time required for the disappearance of spirochetes from the lesions varied according to the plan of treatment and the amount of arsphenamine used. In the first group of patients treated in plan 1, there were only 52.5 per cent negative dark fields after the first day of treatment. With each successive increase in the amount of arsphenamine given the first day there was a greater number of dark field negative cases after twenty-four hours. It was not until we reached the fifth plan, in which each patient received 1.0 Gm. of arsphenamine the first day, that 100 per cent of the dark fields became negative within twenty-four hours from the beginning of treatment, as shown by table 2.

Healing of all surface lesions was prompt and usually complete by the time the patient was discharged from the ward in seven days, irrespective of the plan used. Within twenty-four hours after beginning treatment the open lesions were noticeably drier, swelling was less and epithelization of the chancre was usually complete by the time of discharge. All secondary lesions healed promptly, the macular lesions disappearing within the first one or two days. All lichenoid and papular lesions became flat and healed completely, or practically so, within a week. The enlarged glands were the last to disappear, sometimes requiring two or three months or longer to subside.

Of the 332 cases treated by all plans, we shall discuss only the 178 that have been followed from six months to three years. One hundred and eighteen (66 per cent) are clinically and serologically negative and have normal spinal fluids. Three cases are still serologically positive at nine, ten and eleven months respectively. Their final outcome is pending (table 3).

Fifty-seven patients had an unsatisfactory outcome. Of this number 36 had cutaneous recurrences with recovery of spirochetes on dark field examination. Two of these cases that were dark field positive showed negative blood Wassermann reactions at the time of the recurrence. Also of these 36 cutaneous relapses 24 had become serologically negative for varying periods of time before their recurrence.

Of the 57 patients with unsatisfactory outcome 12 failed to become serologically negative by the end of a year, and 9 patients became negative but reverted to positive.

It will be seen then that of the entire 178 cases only 27 failed to become serologically negative at some time during the observation.

All cases that have not become serologically negative after one year's observation are classed as treatment failures.

Each patient had a spinal fluid examination before the treatment was begun. Of the entire group only 19 were found to have positive spinal Wassermanns in varying degrees. Four of these have become negative, 8 have been lost from observation, 4 had positive spinals at the end of one year and were successfully treated, and the remaining 3 are under observation.

Of the 57 unsuccessfully treated patients, 18 were retreated in the ward with a more intensified plan than was used originally. On the whole they tolerated the treatment better the second time, with the increased amount of drug, than they did originally. Further, it is interesting to note that all these patients except 1 had a Herxheimer reaction on the first or second day of the second course of treatment, with a rise in temperature to 100 F. or over, just as they had had in the first course. Eight of these patients had temperatures that rose to 102 F. or over. One patient had a nitritoid reaction with the first injection of the second course.

None of the relapsed cases that were retreated successfully in the ward have been added to the list of cures. The remaining relapsed cases were treated as ambulatory patients in the clinic. Two cases have had a second relapse.

Of all patients treated 69 are in the armed forces and 38 are in the Merchant Marine. Thirty-nine other patients are from out of the city and are classed as transients. One is in a sanatorium. Five are in defense jobs and are unable to report to the clinic. Three are dead: 1 in the ward, previously referred to, 1 killed in an automobile accident and the third dead from an unknown cause. We have lost 70 patients (20 per cent) from our clinic, and neither the social service department nor the board of health has been able to find them.

Twenty-one white and 4 Negroes, totaling 25 patients, ranging in age from 40 to 64, had an almost perfect follow-up. Forty-eight patients of the entire group treated were under 20 years of age, 42 Negro and 6 white. The latter group has been very difficult to follow.

LABORATORY ARSENIC STUDIES

A daily blood arsenic determination was made on each patient.[8] The specimen was taken each morning before the first treatment. This represented a time interval of fourteen to fifteen hours between injections.

The blood arsenic levels revealed interesting facts which we believe are worthy of special mention. Most of the patients had a blood arsenic content that was normal or only slightly increased on admission, and every patient following the first day of treatment had an increase in arsenic that reached a maximum on the third to the sixth day, depending on the amount of arsenic given in each plan. There was no uniformity in the amount of arsenic retained or in the date on which retention reached its height, even when all patients received the same amount of arsphenamine. There was, however, a definite tendency for a greater retention of arsenic as the age incidence of the individual increased. Moreover, there was in most cases a decrease in the amount of arsenic in the urine of the older patients.

There was also a decided increase in the incidence of reactions in patients 34 to 56 years old, whereas the minimum number of patients showing reactions was under 34.

The young men of both the light weight and the middle weight groups disposed of their arsenic better than did the heavy weight group, as revealed by the arsenic blood level curve. Even though the total amount of arsphenamine was less per kilogram of body weight in the heavy weight group there was greater retention than in the light weight patients who received larger amounts of arsphenamine per kilogram of body weight. This bears out our clinical experience, namely, that dosage cannot be satisfactorily gaged according to body weight. For this reason experimental work for standardization of dosage and the like on selected laboratory animals of relatively uniform physique cannot be carried across to human beings who are so different in build, age, health and so on.

The quantity of arsenic retained was virtually the same on the sixth day of treatment in the patients treated with small ascending doses of arsphenamine as it was in the patients to whom large doses were given on the first day and diminished toward the sixth day. This was true when the same amount of arsenic was given in each procedure.

Three things stood out quite definitely in the study: (1) There was always a retention of arsenic long after cessation of treatment; (2) all reactors showed a greater retention of arsenic and for a longer period of time than nonreactors; (3) the more arsenic received, the greater was the retention.

Patients receiving 1.0 Gm. of arsphenamine every other day for a total of 3.0 Gm. in five days had a definite spiking increasing blood arsenic curve, of the same type in each case.

The complete report of our findings of arsenic in the 332 cases studied will be included in detail in another paper.

TABLE 4.—*Severe Reactions*

Plan variation	1	2	3	4	5	6	7	Total Cases
Cases treated	47	40	60	103	27	18	37	
Encephalitis	1	1	..	..	..	..	..	2
Hepatitis	..	..	1	..	..	..	2	3
Dermatitis	..	..	..	..	..	1	1	2
Persistent neuritis	..	..	1	1	..	1	..	3
Leukopenia	..	1	1	..	..	..	..	2
Death (hepatitis)	..	..	..	..	..	..	1	1

REACTIONS TO TREATMENT

There were 12 severe reactions, 1 ending fatally. These included 2 of encephalitis with recovery, 3 of hepatitis (1 ending in death), 1 in an alcoholic addict, 2 of exfoliative dermatitis (1 mild), 3 of persistent neuritis and 2 of blood dyscrasias (table 4).

The first case of encephalitis appeared early in the experiment in a 20 year old Negro under the first plan of treatment in which the patient was given his injections three times a day for five days, receiving a total of 2.1 Gm. of arsphenamine. He developed a secondary rise in temperature during treatment, and on the second day his temperature reached 102.4 F. His

8. Maechling, E. H., and Flinn, F. B.: Colorimetric Determination of Small Amounts of Arsenic in Biologic Material, J. Lab. & Clin. Med. **15**: 779, 1930. Maechling, E. H.: Separation and Determination of Bismuth and Arsenic in Biologic Material, ibid. **18**: 1058, 1933.

temperature remained elevated and two days after cessation of treatment he had a slight tremor of the fingers, which was most noticeable when he was feeding himself. On the third day aphasia was apparent and he was unable to speak distinctly. He was stuporous, had a blank expression, would not obey commands and could not swallow, so that he had to be fed by stomach tube. He had to be catheterized daily, and his bowels were involuntary. He was given fluid and dextrose by vein. A spinal puncture was not done. On the fourteenth day he began to improve and was discharged thirty-three days after his admission, apparently none the worse for his experience except for urinary urgency. His spinal fluid was negative before treatment and has remained so. His blood Wassermann reaction reverted to negative in two months and has remained so.

The second case of encephalitis appeared eight days after completion of treatment in a 26 year old Puerto Rican. He had received a total of 2.4 Gm. of arsphenamine, given three times a day for six days. He was nauseated and vomited on the last two days of treatment and had a mild nosebleed. His treatment had to be interrupted on the sixth day because of a secondary rise in temperature. Instead of receiving 2.55 Gm. of arsphenamine, as outlined, he received only 2.4 Gm. The temperature reached 104 F. after the treatment was stopped and was followed by a toxic erythema of a pronounced type that had a dark red to an almost cyanotic color with purpura developing distal to where a tourniquet was applied on his arm.

On the fifteenth day of his hospitalization, one day after his temperature had fallen to near normal, he developed a tremor in his hands, more pronounced on feeding himself. Within a period of twelve hours he became aphasic, could not obey commands and could not speak clearly. A lumbar puncture was attempted by another department, during which he had a convulsion. Four cc. of grossly bloody fluid was obtained which was thought to be due to trauma. His treatment consisted of dextrose infusions twice daily and sedation as required. He was semicomatose for four days, when he began to improve. His recovery was complete and he was discharged thirty-three days after his admission, apparently well. His blood Wassermann reaction was negative six months after treatment.

We had no way of foretelling that either patient would have encephalitis until the first signs of tremor appeared, followed later by aphasia.

Of the 3 cases of hepatitis, the first occurred sixty-three days after discharge from the hospital:

He was a chronic alcoholic addict aged 21. His hepatitis followed one of his periodic alcoholic bouts. This patient was in treatment plan 3. He received 2.0 Gm. of arsphenamine and tolerated his treatment well. His liver function tests had been normal on his first admission to the hospital and on subsequent clinic visits. He recovered from his hepatitis after a stay of fifteen days in the hospital. His blood Wassermann reaction became negative and remained so for about one and one-half years before he was taken into the Army.

The second patient, aged 22, developed symptoms of hepatitis three days after receiving 3.2 Gm. of arsphenamine in five days. There was no history of previous icterus or disease of the liver. His temperature rose on the fifth day, and treatment was stopped immediately. His cephalin flocculation tests rose from negative to 4 plus, together with a rise in temperature to 104.4 F., and a toxic erythema. Clinical jaundice was evident three days after treatment had been stopped.

The patient was nauseated throughout his treatment period and vomited. He ate very little food during this time and was given 1,000 cc. of 5 per cent dextrose solution intravenously twice daily, starting with the second day of treatment. His liver became enlarged and tender. The patient complained of pains all over his body and generalized weakness. He had pain also across his chest. The night of the sixth day he had a severe epistaxis, estimated at about 400 cc. His blood pressure rose from 140 systolic to 186 systolic. On the seventh day of his hospitalization he suddenly developed short, fast respirations and tachycardia. The heart and lungs were normal on physical examination except for a high right diaphragm. His temperature fell to 99.4 F. He had to be placed in an oxygen tent. He grew gradually weaker and died on the evening of the ninth day after admission. Permission for postmortem examination could not be obtained.

The third patient, aged 31, showed no clinical evidence of jaundice but the diagnosis was made on the basis of a rise in cephalin flocculation from negative to 3 plus. Also his cholesterol blood level fell to 78 mg. per hundred cubic centimeters. He had a secondary rise in temperature to 102.4 F. and a toxic erythema. His total treatment was 3.2 Gm. of arsphenamine in six days. He had an uneventful recovery after a stay of twenty-one days in the hospital.

A transient leukopenia was observed in 2 patients:

The first was a 25 year old Negro who had received 1.7 Gm. of arsphenamine in six days. His initial leukocyte blood count fell from 5,000 to 2,480 per cubic millimeter and polymorphonuclear leukocytes fell from 74 per cent to 43 per cent. The patient was given three small blood transfusions over a period of ten days. He recovered completely. His only symptom was a daily temperature that fluctuated between 102 and 104 F. The temperature fell to 98.6 F. after the blood transfusions and the blood count became normal. He has remained clinically and serologically negative for over two years.

The second patient with leukopenia, a 28 year old Negro who received 2.4 Gm. of arsphenamine in six days, showed symptoms of agranulocytosis on the seventeenth day after treatment had been stopped. His leukocyte count of 8,560 per cubic millimeter of blood on admission with 70 per cent polymorphonuclear leukocytes fell to 6,400 leukocytes, with an absence of granular forms. Frequent blood counts in this interval revealed a gradual reduction of leukocytes and granulocytes. His recovery was spontaneous, without treatment of any kind, and complete in two and a half weeks. He too has been serologically and clinically negative for more than a year.

Three patients with severe neuritis have been persistent for approximately nine months, one year and one and one-half years respectively. Their ages were 26, 31 and 34 years, and they received 3.4 Gm., 2.0 Gm. and 3.0 Gm. respectively. Each patient complained of "pins and needles" sensation in the feet. They also had dull pain in the calves and knees. There was no ataxia. Two patients have continued to work. The third patient has an active pulmonary tuberculosis and is now confined to a sanatorium with that disease. All 3 are still serologically and clinically negative.

Of 2 patients with exfoliative dermatitis, the first patient, aged 33, developed dermatitis ten days after he was discharged from the hospital. He received 3.6 Gm. of arsphenamine. Treatment was discontinued on the fifth day because of a rise in temperature followed by a toxic erythema. He was discharged on the fourteenth day, well except for a little itching of the forearms and flanks. After being out of the hospital ten days he developed a generalized exudative dermatitis accompanied by edema. He was readmitted and hospitalized for three weeks. He had general thinning of hair and exfoliating of all nails. This patient has remained clinically and serologically cured for approximately eight months of observation.

The second case of dermatitis developed fourteen days after discharge from the hospital. A man aged 33 was in the seventh treatment plan and tolerated his drug well except for a pain in the pit of his stomach on the last day. His total dose was 3.9 Gm. of arsphenamine. This patient had a dry, itching, lichenified eruption that was generalized, with a few areas of exudation. He remained ambulatory and the condition cleared in approximately three weeks without any other symptoms.

There were numerous minor reactions, such as an initial rise in temperature the first day that appeared in a great majority of cases and returned to normal the

next day. Although the temperature may have risen to 104 F. in the first afternoon, the regular injection of arsphenamine was given and the temperature would be normal the next day. Patients with secondary syphilitic manifestations often had redness and swelling of the surface lesions and tenderness of the glands. These too disappeared the following morning.

Secondary rises in temperature and toxic erythemas occurred near the end of the course, and mild neuritis usually appeared about two weeks after cessation of treatment. The neuritis was evidenced by transitory numbness and tingling of the hands and feet that usually cleared in a few days to several weeks.

The aforementioned reactions were the ones most commonly encountered, the incidence of their frequency increasing as the amount of the drug was increased. The occurrence of rise in secondary temperature over 100 F. was 25 per cent in the first group treated and increased to 89 per cent in patients receiving the greatest amount of arsphenamine. Mild neuritis rose from 2 per cent to 35 per cent. Toxic erythemas increased from 8 per cent to 40 per cent. All toxic erythemas were preceded by a rise in temperature of 100 F. or over.

These reactions, as a rule, were of no serious import and often were so mild as not to have been noticed by the patient or were brought out only on close questioning.

Traces of albumin were noted in the urine in 18 per cent of the cases. Ten cases showed as much as 3 plus albumin in the urine (based on 1 plus to 4 plus reaction). All these subsequently cleared following completion of treatment. Albumin, which was found in the urine of 7 patients before treatment was begun, disappeared completely in 5 of the cases during the course of the treatment.

Jaundice, without evidence of hepatitis, as demonstrated by negative cephalin flocculation reactions, was observed in 3 patients following toxic erythemas. Their recoveries were complete.

Vomiting at some time during the course of the treatment occurred in 22 per cent of the cases. Diarrhea, when present, usually occurred on the first day and was present in 10 per cent of the cases.

Still milder reactions included anorexia, nausea, abdominal pain, transient pruritus, herpes simplex, epistaxis, watering of the eyes, buzzing of the ears, herpes zoster and herpes progenitalis. All were transient.

OBSERVATIONS

A study of approximately 2,500 titrated Wassermann reactions showed that the higher the titer the longer the time required for the Wassermann reaction to become negative; the weaker the titer, the shorter the time. Patients with the highest titer, i. e. positive reaction in a dilution of 1:160 of the whole serum, required an average of twenty-two weeks to become negative and to continue so. Cases with titers positive in a 1:80 dilution required an average of fifteen weeks to become negative; those with 1:40 dilution, fourteen weeks; 1:20 dilution, eleven weeks, while those with a 1:10 dilution required 9.7 weeks to become negative. Cases showing a 4 plus reaction with a negative titer required an average of 8.9 weeks, while those with a 1 plus to 3 plus Wassermann reaction required only 4.1 weeks to reverse. The patients with seronegative primaries in which the blood Wassermann reaction became positive during the treatment required 4.4 weeks to become completely negative again.

Those patients having positive titers greater than the usual 4 plus in undiluted serum were not only more resistant to treatment but had more than twice the number of recurrences than were found in the cases in which the initial blood Wassermann reaction was 4 plus or less: 37.2 per cent in the former as compared to 14.2 per cent in the latter.

These findings indicate that the earlier the treatment is begun in the syphilitic, preferably before the Wassermann reaction becomes positive (seronegative primary), the greater the chances of cure. One would infer that a patient whose blood Wassermann reaction does not become negative within six months from the beginning of intensive arsenotherapy and remain so should in all probability be considered inadequately treated.

The foregoing observations suggest that a syphilitic patient who becomes serologically negative after the expiration of six months from the date of his last treatment does so by the retention of arsenic or by his own body resistance.

TABLE 5.—*Moderate Reactions*

Plan variation	1	2	3	4	5	6	7
Cases treated	47	40	60	103	27	18	37
Primary rise in temp.	72.5%	82.5%	90.0%	80.5%	96.3%	94.4%	94.5%
Secondary rise in temp.	25.5%	22.5%	33.3%	34.4%	44.5%	89.0%	89.2%
Toxic erythema Milian	8.5	12.5	16.6	22.3	14.8	55.5	35.7
Transient neuritis	2.1	7.5	11.4	12.6	14.8	33.3	28.5

TABLE 6.—*Weeks for Blood Wassermann Reaction to Become Negative*

Positive on Admission	Weeks to Become Negative
1/160 dilution titer	22
1/80 dilution titer	15
1/40 dilution titer	14
1/20 dilution titer	11
1/10 dilution titer	9.7
Four plus in undiluted serum	8.9
One plus to 3 plus in undiluted serum	4.1
Negative that became positive during treatment	4.4

Fifty-nine patients who were over 33 years of age became and have remained serologically and clinically cured to date with the exception of 3, and the latter patients had only serologic relapses. The fact that this same age group showed the greatest retention of arsenic would tend to substantiate our belief that the patients who became spontaneously cured long after cessation of treatment did so by the arsenic stored in their systems.

The percentage of cures was the same in patients who received a total of 3.0 Gm. of arsphenamine given in 1.0 Gm. doses on alternate days as in the patients receiving the same total amount of arsphenamine given daily.

The patients who received the largest dosage of arsphenamine (70 mg. per kilogram of body weight) had no reactions either while under treatment or subsequently and to date have remained serologically and clinically negative.

All patients receiving 1.0 Gm. of arsphenamine the first day were dark field negative within twenty-four hours after their first injection.

Sixty-one patients had seronegative primary lesions, 47 of whom reverted to positive while under treatment.

A large dose of arsphenamine on the first day of treatment in early syphilis was more effective than a small dose in rendering the lesions dark field negative, and the serious toxic reactions were no greater.

The greater the amount of arsphenamine given, the more frequent was the occurrence of primary fever and secondary fever, and the more severe the toxic erythema, nausea, vomiting, neuritis and dermatitis.

Patients reacting with fever or toxic erythemas showed no higher percentage of cures than those without such reactions.

All 12 patients who had severe reactions, hepatitis, encephalitis, dermatitis, blood dyscrasias and neuritis became serologically negative and have remained so.

Twenty-eight per cent of patients who had neuritis had symptoms within one week after finishing the treatment.

Both cases of encephalitis occurred with relatively small doses of arsphenamine, 2.1 and 2.4 Gm. respectively, given in fractional doses three times a day in the five and six day plans. Neither patient had spinal drainage, and both recovered.

Patients in the light weight groups who received the smallest amount of arsphenamine had the fewest number of cures.

Of the 36 mucocutaneous recurrences, 10 showed chancres with enlargement of the regional glands and recovery of spirochetes from the chancre. Some initial lesions were located at different sites from the original chancre. There was no way to distinguish the lesions in the recurring mucocutaneous relapses from those observed in the original infection.

No case of thrombocytopenic purpura was found clinically, nor was there a depression in the platelet counts that were done repeatedly on all patients.

Patients receiving over 55 mg. of arsphenamine per kilogram of body weight had the most satisfactory outcome.

Of the entire series treated, only 27 patients failed to become serologically negative.

SUMMARY

Three hundred and thirty-two patients with early syphilis were treated three or four times daily over five or six day periods with arsphenamine by the syringe method.

Of 178 patients followed for six months to approximately three years, 118 have remained clinically cured with negative blood Wassermann and spinal fluids.

Fifty-seven patients had unsatisfactory outcomes. Thirty-six of these had mucocutaneous relapses with recovery of spirochetes.

There was one death from toxic hepatitis. Two patients had encephalitis, 3 hepatitis, including the one mentioned, 3 severe neuritis, 2 exfoliating dermatitis and 2 blood dyscrasias.

CONCLUSIONS

As a result of our experience in this study we are forced to the opinion that treatment of early syphilis with arsphenamine by the multiple syringe method over a period of five or six days is ineffective, dangerous, expensive and altogether unpractical.

We are convinced that any such five or six day intensive treatment plan with arsphenamine, using the multiple syringe method, must be followed by additional therapy of a heavy metal, fever or both to be successful.

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COMBINED FEVER AND ARSENOTHERAPY

IN THE INTENSIVE TREATMENT OF EARLY SYPHILIS

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Since Ehrlich's discovery of arsphenamine, the treatment of syphilis by the intensive use of arsenical drugs has been associated with the hazard of toxic reactions. The introduction of arsenoxide, which permitted smaller doses of arsenic with equally good therapeutic results, lowered the incidence of toxic effects but failed to eliminate them.

Eagle and Hogan [1] in their reports on the toxicity of arsenoxide, calculated from experiments in animals, showed that the margin of safety in man was only about 3.0 when a total dose of 1,200 mg. of mapharsen was given to the average adult in five to ten days. They considered this margin of safety dangerously low. When mapharsen alone is used in the rapid treatment of syphilis, clinical experience indicates that a total of 20 to 30 mg. per kilogram of body weight is needed for the best results. From our experience at Bellevue Hospital, Eagle and Hogan were correct in considering a schedule of therapy requiring this amount of mapharsen in a five to ten day period too dangerous for routine use.

A false sense of security can easily be acquired in intensive arsenotherapy, because one may give a hundred treatment courses with relatively large amounts of mapharsen and encounter no serious difficulty only to be rudely awakened by a grave reaction in the very next treatment. So far no one has collected into a single statistical table all of the available data on the toxic effects of intensive arsenotherapy. When this is done for treatment schedules where mapharsen alone was given in five to ten days, it will probably be found that the incidence of encephalopathy has been over 1 per cent. This at least was our experience at Bellevue Hospital.

Following our first death from arsenical encephalopathy, we tried lowering the total dose of mapharsen and turned to fever to reinforce the action of these lowered doses. Originally we believed that the combination of fever with chemotherapy not only would permit smaller amounts of mapharsen but might also protect against its toxicity, as Rose, Simpson and Kendell [2] suggested. Consequently we completed several relatively large series of treatment courses using various combinations of mapharsen with fever induced by typhoid vaccine. Every one of these schedules called for two injections of about 60 mg. of mapharsen

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1. Eagle, H., and Hogan, R. B.: An Experimental Evaluation of Intensive Methods for the Treatment of Early Syphilis, Ven. Dis. Inform. **24**: 33, 69 and 159, 1943.

2. Rose, D. L.; Simpson, W. M., and Kendell, H. W.: Quantitative Serologic Studies in Early Syphilis: III. Treatment with a Single Intensive Session of Combined Fever-Chemotherapy, Ven. Dis. Inform. **23**: 411, 1942.

on at least one day of treatment. The incidence of arsenical encephalopathy, however, continued to be over 1 per cent, although most of the reactions were less severe because of the lower total dose of mapharsen. Thus it was evident that fever failed to protect against the toxicity of arsenic. And, in fact, Carpenter and his co-workers [3] recently have reported that in animals fever actually increases the toxicity of mapharsen; but it also enhances the effectiveness of arsenotherapy and so permits smaller amounts of drug.

Table 1 shows that among 321 treatment courses given at Bellevue Hospital with mapharsen alone in a six to ten day period the incidence of encephalopathy was 1.6 per cent. In a series of 588 treatment courses with combined fever and mapharsen in which two injections of about 60 mg. of mapharsen were given on at least one day of treatment, the incidence of encephalopathy was 1.36 per cent. In the total series of 909 treatment courses encephalopathy occurred in 1.43 per cent and the mortality rate was 1 in 300.

The advantages of rapid treatment for early syphilis to both the community and the patient are so great that one might justify even a mortality of 0.3 per cent if safer means of rapid cure were unavailable. But obviously our task was to find safer schedules of treatment. As we have as yet no means of determining in advance the tolerance of individuals for arsenical drugs, we attempted to find the dose of mapharsen which could be given in five to ten days without danger to those particularly susceptible to arsenic. To determine this as well as the effectiveness of the therapy, it was necessary to give relatively large series of treatment courses. A death attributed to treatment made us change the schedule of therapy, but it was not until after our third fatality that we finally found a method of treatment which proved acceptable.

In formulating our schedules of therapy we had to consider not only the total amount of mapharsen which could safely be given in five to ten days but also the maximum single dose which could prudently be given at daily intervals. By July 1942 we determined that the maximum single dose of mapharsen per day was approximately 1 mg. per kilogram of body weight and the minimum period of treatment was ten days. With this schedule the average patient received ten daily injections of about 60 mg. of mapharsen. To reinforce treatment with this low dosage, four fevers induced by typhoid vaccine were included in the ten days.

The fevers as a rule were given on the second, fourth, sixth and eighth days. The vaccine used was obtained from the New York City Department of Health and contained 1,000 million B. typhosus, 750 million B. paratyphosus A and 750 million B. paratyphosus B. per cubic centimeter. The first fever was induced with an initial injection of 0.1 cc. of this vaccine intravenously, the second with 0.2 cc., the third with 0.4 cc. and the last with 0.6 cc. From one and one-half to two hours after the initial injection another dose was given of equal amount in most cases. The response to these injections varied, but in general these doses caused a fever of at least 104 F. for about four hours.

The induction of fever with typhoid vaccine causes discomfort to patients, but this can usually be alleviated with sedatives, such as isonipecaine or, if necessary, morphine. In our opinion the induction of fever with typhoid vaccine is safer than with electropyrexia. The latter is more effective therapeutically, because more sustained and higher fevers can be produced, but it is less practical because the necessary equipment and personnel for inducing fevers with electropyrexia are not usually available. At Bellevue Hospital we have given typhoid vaccine intravenously in over 1,650 treatment courses without a single serious reaction due to the vaccine.

In June 1943, further to enhance the effect of treatment, we added bismuth to our schedule of rapid treatment, giving intramuscular injections of 0.1 Gm. of bismuth salicylate in oil on the first, third, seventh and tenth days of therapy. Thus, our standard chart of therapy came to be as shown in table 2.

By May 1, 1944 we had given 1,163 treatment courses according to this plan without a single fatality. Only 3 very mild cases of encephalopathy were encountered. The diagnosis in all 3 was made chiefly by finding increased cells and protein in the spinal fluid. One patient developed an agranulocytosis, with complete recovery after a single transfusion with whole blood.

TABLE 1.—*Cerebral Reactions*

	Mapharsen Only	Mapharsen and Typhoid 7-8 Day Treatment	Total
Number of treatment courses.....	321	588	909
Encephalopathy.....	5 (1.6%)	8 (1.36%)	13 (1.43%)
Deaths.....	1 (0.3%)	2 (0.34%)	3 (0.33%)

TABLE 2.—*Ten Day Plan of Treatment*

	1	2	3	4	5	6	7	8	9	10
Mapharsen, 1 mg. per kilogram...	×	×	×	×	×	×	×	×	×	×
Bismuth salicylate in oil, 100 mg..	×		×				×			×
Typhoid vaccine in cubic centimeters.....	0.1		0.2		0.4		0.6			

Unfortunately, this record was broken even as this paper was being written. On May 5, 1944 a white woman with secondary syphilis, who was six months pregnant, developed encephalopathy following her fifth injection of 70 mg. of mapharsen and died. During the five days of treatment she had had only one fever induced by typhoid vaccine. This tragic accident again shows that, when arsenical drugs are used, there is always the danger of a fatal accident in a person who has a definite sensitivity to arsenic. Fatal arsenical encephalopathy has occurred after only two injections of neoarsphenamine given five days apart; and as long as syphilis is treated with arsenic the rule of constant alertness by those administering the treatment can never be broken. Arsenical encephalopathy strikes like a bolt from the blue, but in many cases fatal reactions can be prevented by the caution which comes from experience. We have found that the apprehensive, worrying type of individual demands special attention. It is also probable that pregnancy adds to the risk of intensive arsenotherapy. Our recent fatality occurred in a woman who was both apprehensive and pregnant. In addition, her treatment was started at a time of confusion, when the syphilis service at Bellevue Hospital was being moved to new quarters.

By May 15, 1944 we had completed 1,181 treatment courses with the schedule of therapy we had adopted in July 1942. On this schedule the incidence of serious

3. Jones, N.; Carpenter, C. M.; Boak, R. A.; Warren, S. L., and Hanson, H.: The One Day Treatment of Syphilis with Fever and Mapharsen, Ven. Dis. Inform. **25**: 99, 1944.

reactions is very low. As shown in table 3, the incidence of encephalopathy among our patients dropped from 1.43 per cent to 0.34 and the mortality rate is 1 in 1,181 instead of 1 in 300. Since our latest and, we hope, our last fatality we have slightly modified the schedule of treatment so that the mapharsen is injected in the late afternoon instead of the morning. This means that on the fever days the injection of mapharsen follows the fever instead of preceding it.

RESULTS OF TREATMENT

In compiling statistical results of treatment we have chosen six months as the minimum follow-up period which is likely to give a fairly accurate estimate of the effectiveness of the treatment. This period has been chosen both because the serologic tests of most patients with early syphilis become negative within six months after effective rapid therapy and because the majority of relapses occur within this period. A careful analysis of all the relapses or reinfections which have come to our attention at Bellevue Hospital following rapid treatment for early syphilis makes us hesitate to distinguish between relapses and reinfections in compiling statistical tables. We believe that reinfections are much more frequent than relapses after six months. Consequently an observation period of six months enables us to differentiate somewhat between a fairly valuable follow-up and one that is less revealing of the probable results of treatment.

TABLE 3.—*Cerebral Reactions in Ten Day Treatment*

Number of treatment courses	1,181
Encephalopathy	4 (0.34%)
Deaths	1 (0.08%)

TABLE 4.—*Results of Ten Day Treatment*

	Total	
	Number	Per Cent
Status of patients followed:		
Lost (followed less than 6 months)	337	43.7
Number followed 6 to 38 months	435	56.3
Total number treated	772	100.0
Probable favorable results:		
Negative serologic reactions	304	69.9
Wassermann titers less than 8	47	10.8
Probable favorable results (total number)	351	80.7
Unfavorable results:		
Relapse or reinfection	59	13.6
Wassermann titers greater than 8	25	5.7
Unfavorable results (total number)	84	19.3
Total number followed	435	100

We excluded from the analysis of therapeutic results all patients lost within the first six months of follow-up, regardless of whether or not they had negative serologic tests when last seen. Patients with Wassermann titers less than 8, as reported by the New York State Department of Health serologic laboratory, are included among those with a satisfactory status because experience has proved that almost all such patients go on to become seronegative. Patients with Wassermann titers greater than 8 six months or more after treatment are reported as unsatisfactory results, although some of them may become seronegative without further treatment. This method of reporting is based on over four years of experience in observing quantitative serologic tests for syphilis. From our experience, as long as Wassermann titers of the blood are falling or remain at low levels, further treatment is not indicated.

As our case load at Bellevue Hospital has increased decidedly since August 1943, many patients treated according to the schedule of therapy we have just described have been followed for too short a period to be included in the present tabulation of results. It should also be stated that most of the patients on whom treatment results are reported did not receive bismuth in addition to mapharsen and fever. The percentage of patients kept under observation is not as high in this group as in previous groups, partly because of the increased case load but chiefly because of the increased number of sailors and transients admitted to the hospital for the rapid treatment of early syphilis.

Included among the treatment results summarized in table 4 is a relatively small group of patients who received a total of 0.54 Gm. of mapharsen and four fevers induced by typhoid vaccine prior to July 1942. This group is included because the treatment was similar and because the patients in it have been followed for longer periods.

The percentage of satisfactory results reported in table 4 is not quite as high as for most of the schedules of treatment published in our previous reports,[4] but the differences are not very significant and the percentage of 80.7 satisfactory results is almost identical with that given in a recent report by Schoch and Alexander,[5] who used much larger doses of mapharsen without the addition of fever.

138 East 36th Street.

ABSTRACT OF DISCUSSION

ON PAPERS OF DR. EAGLE, DRS. CANNON, FISHER, RODRIGUEZ, BEATTIE AND MAECHLING AND DRS. THOMAS AND WEXLER

DR. HERBERT RATTNER, Chicago: It is eleven years since Dr. Chargin and his associates introduced the five day treatment with neoarsphenamine. Since then many modifications of the original method have been introduced: the one day arsenofever method, which received so much premature publicity but of which little is heard today; the use of arsenic and bismuth administered concurrently in a course of five days; the syringe method, in which the drug is administered in seven, ten or twenty days, and the three methods reported today. Dr. Cannon concluded that his method had little merit. The methods of Eagle and Thomas are equally effective with respect to their "curative" values. With both methods there was an incidence of about 1:1,200 of fatal reactions. Thomas's fatality occurred in a pregnant woman, and he suggests therefore that pregnancy adds to the risk of intensive arsenotherapy. At our hospital we treated 29 pregnant women in all stages of pregnancy by the five day method without a serious reaction, and in each case there was a normal baby. With the method of Thomas the patient is isolated, rendered noninfectious quickly, wilful lapse from treatment is reduced to a minimum, and untoward reactions can be treated early. With Eagle's routine the patient continues at work, but inevitably when one relies on a patient to return of his own will there results a high lapse rate. Apparently any rapid method will cure the majority of patients who receive a sufficient amount of drug. Statistics indicate that the shorter the course of treatment, the greater the element of risk, but there are times when one must assume the risk. At the Cook County Hospital we used the five day method on 480 patients without a fatality. We attribute these good results in part to our willingness to discontinue treatment temporarily for the smallest reason—persistent headache, nausea or fever, and in such cases concentrated glucose was administered liberally.

4. Thomas, E. W., and Wexler, G.: Rapid Treatment of Early Syphilis with Multiple Injections of Mapharsen, Am. J. Pub. Health **31**: 545, 1941; Rapid Treatment of Early Syphilis, Arch. Dermat. & Syph. **47**: 553 (April) 1943.

5. Schoch, A. G., and Alexander, L. J.: Infections and Serologic Relapse During Intensive Arsenotherapy of Early Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **28**: 221, 1944.

There are available to the physician a number of methods from which to choose that which is best suited to the patient's needs. Dr. Thomas's method is excellent for public practice. For the private patient who can be trusted to return for treatment, the Eagle method may be safer. For the traveling man who has but a week to give to treatment the five day treatment is eminently suitable. And if he wishes that there be no hospital record, one could use the Schoch syringe technic.

DR. E. A. STRAKOSCH, Chicago: From Oct. 31, 1942 through April 30, 1944 we started 515 patients on the Eagle-Hogan regimen at the Chicago Intensive Treatment Center. These were patients with primary, secondary or early latent syphilis who, on account of heart, chest or other pathologic findings, were ruled out from intensive fever-chemotherapy or the modification of the Schoch-Alexander treatment; 470 patients were started on the eight weeks and only 45 on the ten weeks schedule. It is noteworthy that only 211 patients completed their treatment. Of the 211, only 58 completed it on time; 132 patients became delinquent; 57 patients moved out of our jurisdiction—Army, Navy or somewhere else—and 103 patients stayed under our treatment. The range of delinquency goes up to 204 days. The treatment had to be discontinued in 12 patients because of nephrosis in 1 case, hepatitis after the fifth arsenic injection in another and severe bismuth stomatitis in 9 cases, and because of an uncooperative attitude in another. Seven patients were retreated: 1 with primary syphilis on account of serologic progression, 4 patients with secondary syphilis, 2 on account of cutaneous relapses, 2 on account of serologic relapse and 2 patients with latent syphilis whose Kahn titer was still positive or unchanged six months after the treatment was finished. These 7 patients took their treatment irregularly and did not finish it in time. It is my opinion that the Eagle-Hogan treatment method is a more practical, safer and to some extent better method than the other methods used by us, such as the fever-chemotherapy or the Schoch-Alexander method or its modifications. The definite disadvantage is the high treatment delinquency even in a treatment schedule as short as eight weeks.

DR. ARTHUR CURTIS, Ann Arbor, Mich.: By far the most serious complication of massive arsenotherapy is hemorrhagic encephalitis. Last fall Dr. Mallery and I, hoping to find some procedure which might enable us to anticipate the development of hemorrhagic encephalitis, set up the following experiment for patients receiving intensive arsenotherapy: On the day before treatment was begun, the first day of treatment, the third day of treatment and the fifth day of treatment, as well as two days after treatment ceased, the following procedures were done: a complete blood count, bleeding time, clotting time, prothrombin time, vitamin C level, positive pressure tourniquet test (Rumpel-Leede) and a negative pressure test. With these procedures we followed 58 consecutive patients on massive arsenotherapy. During this period there were 7 cases of hemorrhagic encephalitis with 2 fatalities. All patients that developed hemorrhagic encephalitis, with the exception of 1 male, had a positive pressure tourniquet test (Rumpel-Leede) before the onset of clinical symptoms. Since that time we have used the positive pressure tourniquet test (Rumpel-Leede) on all of our patients receiving intensive arsenotherapy. Treatment is stopped immediately on the appearance of any petechial hemorrhage by this test. We have not had a case of hemorrhagic encephalitis since that time.

DR. GEORGE X. SCHWEMLEIN, Chicago: The Section on Fever-Chemotherapy at the Chicago Intensive Treatment Center is continuing the study of the use of artificial fever combined with chemotherapy in early syphilis. Past experiences have demonstrated that this type of therapy has been beneficial in neurosyphilis and congenital and ocular syphilis; it was a natural step to investigate the effect of this procedure on the early stages of syphilis. We have employed a single eight hour session of artificial fever at 105 to 106 F. rectal level, with varying amounts of mapharsen and bismuth. On the basis of 1,500 patients treated the following observations may be noted: Combined artificial fever-chemotherapy is effective in completely arresting the disease; the method is advantageous in that relatively small amounts of mapharsen and bismuth are employed; the use of physically induced fever is as satisfactory as other methods; from the public health standpoint infectious syphilis can be quickly controlled in the vast majority of cases.

DR. J. R. DRIVER, Cleveland: It has been shown here today that a large proportion of patients treated for early infectious syphilis by short, intensive methods can be rendered noninfectious and probably cured. However, these methods are still experimental, are attended by more risks than the standard treatment procedures and should be used only by experts. Justification for their use lies chiefly in the control of large groups of early syphilitic infections that present a public health hazard especially in our large urban centers. The great majority of syphilitic infections occur among the most ignorant and least cooperative of our population. The difficulty in the past has been to keep them under treatment long enough to render them noninfectious. Therefore the desirability of intensive treatment procedures is obvious. With the Eagle method the patients are treated in the outpatient clinics, and the lapse rate due to uncooperative behavior is higher. In our treatment centers at the university hospitals and at the Cleveland City Hospital, out of 178 cases in which treatment was begun, completion of treatment was obtained in only 92. A few of these were given other forms of treatment because of vacations, but the great majority were lost as a result of uncooperative behavior. The advantage of the Thomas method lies in the fact that the patients are hospitalized during the entire course of treatment. Out of 252 cases in which we have begun treatment by this method, the course has been completed in 243. In 9 cases other forms of therapy were instituted because of severe reactions. In only 1 instance was treatment discontinued because of uncooperative behavior.

DR. ROY L. KILE, Cleveland: Dr. Driver has explained the series of cases we have observed in Cleveland on the Thomas-Wexler routine. There was one death, which Dr. George Blinkley observed, wherein a batch of mapharsen was used that was outdated. This was the only serious reaction in 266 cases treated by this routine. I want to call attention to the fact that there may be some variation in different batches of mapharsen, more reactions having been noted with certain ones. The results with the Thomas-Wexler routine have been very satisfactory. The patients are hospitalized during their treatment and are free to return to work in a comparatively short time.

DR. ARTHUR G. SCHOCH, Dallas, Texas: The addition of bismuth to any arsenical regimen for the treatment of early syphilis seems to be a necessity. We thought that the addition of a rapidly acting oil soluble bismuth, bismuth ethyl camphorate, should be one step beyond the use of the slowly acting insoluble bismuth salicylate in oil. So far our results have been very encouraging. Using the Eagle triweekly schedule and substituting bismuth ethyl camphorate for bismuth saljcylate, appraising results on patients who have been followed for at least eight months or longer, our failure group is 5.3 per cent. Our successes in that particular group, which totals 131, are 94.7 per cent.

DR. HARRY EAGLE, SURGEON, U. S. P. H. S.: The point has been raised as to the differentiation between reinfection and relapse in treated cases of early syphilis. The distinction is so difficult and the final decision is often so arbitrary that in the evaluation of a new therapeutic procedure any treated case in which dark field positive lesions develop within one to two years must be adjudged a treatment failure unless the evidence for reinfection is overwhelming. Those who are studying the intensive treatment of early syphilis are not necessarily protagonists of a particular procedure to the exclusion of all others. There are indications for highly intensive arsenotherapy and indications for more conservative treatment, and the correct procedure to be followed in the individual case must be decided by the physician on its own merits. There is no universally applicable method of choice. The best record will be given by a highly intensive procedure applied to a hospitalized patient. On the triweekly schedule I have described a certain proportion of patients will necessarily be lost, but the case holding record will be better than with routine weekly treatment continued for a year and a half. It is impossible to estimate precisely what the case holding record has been in our own study, because the duration of the scheduled treatment has deliberately been varied. Moreover, the proportion of patients completing their scheduled treatment has varied from as high as 90 per cent in some clinics to as low as 20 per cent in others. The degree to which patients

lapse is affected by many variables, a few of which are the type of patient, the efficiency of the social service workers and the quality of the medical care in the clinic itself. On a triweekly schedule more patients will receive an adequate amount of treatment than is the case with a weekly schedule but less than with a schedule involving hospitalization. In analyzing our results, no attempt was made to distinguish between the efficacy of the various types of bismuth preparation. Eighty per cent of the patients received bismuth subsalicylate and more than 90 per cent of those received 0.2 Gm. per weekly injection. Our experimental data indicate that, except for a possible slight superiority of an oil soluble preparation, there is but little difference in the therapeutic efficacy of the several types of bismuth preparations in current use.

DR. JEROME K. FISHER, New York: I realize that a paper as pessimistic as ours doesn't leave much room for comment. With the advent of penicillin and the extensive use of phenarsine compounds in intensive treatment of early syphilis, you have likely heard the swan song of arsphenamine. Our report has been based on all the cases, and those include the cases in which we gave only 1.5 Gm. The treatment of the cases in the sixth variation of our plan, all of which we have followed for six months or longer, has been 100 per cent effective. Our study showed that not all patients require the same amount of arsphenamine. In our early studies we had secondary cases that cleared completely and have been negative for over two years with 1.5 Gm. of arsphenamine. In our later group we had 2 seronegative primary cases in which 3.2 and 3.4 Gm. of arsphenamine were administered in six days which later became seropositive, with lesions and spirochetes recovered. Another fact brought out in our paper is that the largest doses of arsphenamine can be given in the first few days of treatment when the patient is in the best condition. That was the reason for the reversing of our schedule, so that in the allotted time, should a patient be ill, he would have the greatest quantity in his system. We retreated 18 patients. None of these have been included in the present report as having a second course of treatment or have been entered into any of the calculations. Of those 18 cases, all but 1 presented a Herxheimer reaction on the first day of the second course of treatment. In 8 of them the temperature ranged from 102 to 104 F. The paper, although unfavorable so far as the outcome of the use of arsphenamine is concerned, offers a great deal of other information, which unfortunately Dr. Cannon did not have time to include. I think that this will be of value in estimating other plans of intensive treatment, perhaps with penicillin.

DR. EVAN W. THOMAS, New York: With reference to reinfection and relapses, I agree heartily with Dr. Eagle that we must be very conservative. Of the relapses listed in the table which I showed, 12 were seronegative at the time they reappeared with dark field positive lesions. Those, I presume, might be listed as reinfections. However, we have other patients who were followed for thirty months or more. These patients came in with dark field positive lesions after they had been negative for over twenty-six months. They gave histories of promiscuous exposures. They were undoubtedly reinfections, but they were not seronegative at the time they came back. When I discussed the relapses and reinfections in my series, there was not agreement in every case. If you permit any particular person to decide which is a relapse and which is a reinfection, you may get into trouble. I was interested in what Dr. Bruyere said about the age groups. I wonder if it isn't possible that the much higher incidence of relapses in the younger age group is due to the fact that in the younger age group there were many more reinfections than there were in the old age group. It seems to me that is the most plausible explanation. It is exceedingly difficult to get a high follow-up percentage when you deal with Harlem patients in New York City. Nothing caused us such trouble or gave so much work as that follow-up. We still have under observation about 55 per cent of the patients treated in 1940, which I think is extraordinary for New York City. Of this last group only something like 53 per cent were followed over six months. We are now treating many Dutch, Scandinavian and English sailors. It is impossible, no matter what the follow-up system may be, to follow those patients.

MASSIVE ARSENOTHERAPY FOR SYPHILIS

UNITED STATES PUBLIC HEALTH SERVICE EVALUATION

COOPERATING CLINICS OF NEW YORK AND MIDWESTERN GROUPS

Since the first experiments with massive arsenotherapy for syphilis using neoarsphenamine by slow intravenous drip, many methods of intensive treatment have been developed. The present study is concerned with a group of 4,351 intensive treatments for early syphilis contributed to the U. S. Public Health Service Field Study of Massive Arsenotherapy by the twenty-two cooperating clinics listed in table 1. This group of patients is limited to cases in the first four years of infection with or without active manifestations, treated during the period 1933-1943 inclusive. However, the analysis of results deals only with cases in which there was active evidence of primary or secondary syphilis. Six different schemes of treatment were employed, as shown in table 2.

TABLE 1.—*Hospitals Cooperating in the U. S. P. H. S. Field Study of Massive Arsenotherapy for Syphilis, and the Number of Cases of Early Syphilis Contributed to the Study by Each*

Name and Location of Hospital	Cases of Early Syphilis Treated
Bellevue Hospital, New York City	1,054
Long Island College Hospital, Brooklyn	57
Mount Sinai Hospital, New York City	402
New Haven Hospital, New Haven, Conn.	13
Presbyterian Hospital, New York City	258
Riker's Island Prison Hospital, New York City	25
Sing Sing Prison Hospital, Ossining, N. Y.	36
Broadlawns Hospital, Des Moines, Iowa	91
Cleveland City Hospital, Cleveland	10
Coles County Free Treatment Center, Mattoon, Ill.	5
Cook County Hospital, Chicago	463
East Side Health District, East St. Louis, Ill.	2
Henry Ford Hospital, Detroit	20
Herman Kiefer Hospital, Detroit	417
Indianapolis City Hospital, Indianapolis	500
Isolation Hospital, St. Louis	431
Louisville General Hospital, Louisville, Ky.	134
University of Minnesota Hospital, Minneapolis	36
St. Elizabeth's Hospital, Belleville, Ill.	26
St. Joseph's Hospital, Bloomington, Ill.	2
State General Hospital, Madison, Wis.	12
University Hospital, Ann Arbor, Mich.	297
Total, all hospitals	4,351

The follow-up observation on the cases studied was far from complete, but it was adequate for purposes of analysis. As shown in table 3, 18 per cent of the cases were not seen after discharge from the hospital, two thirds were not seen more than one year after treatment, and 85 per cent were not followed beyond the second year.[1] From the point of view of analysis of treatment results as affected by the adequacy of follow-up, it is of interest to note that only half of the secondary recurrences observed occurred in the first six months

Prepared under the direction of Miss Lida J. Usilton, Principal Statistician, with the assistance of Dr. Paul T. Bruyere and Mrs. Martha C. Bruyere, Statistical Section, Venereal Disease Division, U. S. Public Health Service.

Surgeon David C. Elliott, U. S. Public Health Service, was responsible for the promotion, organization and carrying through of this cooperative endeavor, reporting in THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, Oct. 4, 1941, page 1160, the early progress on results of massive arsenotherapy for syphilis for the Midwestern and New York groups.

1. A considerable part of the cases were treated in 1942 and 1943 and hence could not have been observed as long as two years.

after treatment, and that as many as 12 per cent occurred more than one year after treatment.

In evaluating the results obtained, four broad groups were defined as "final outcomes": 1. A case negative for at least three months when last seen was considered to have experienced a "satisfactory result." 2. A case still positive or fluctuating when last seen a year or more after treatment was considered to be "serologically fast." (A fluctuating case was defined to be 1 in which the serologic test on the blood had been negative at some time after treatment, but never for as long as three consecutive months, and had subsequently become positive. The last observation might be either positive or negative.) 3. A case positive or fluctuating at last observation which had previouly fulfilled the criteria for satisfactory result was considered to be a "serologic relapse." 4. A case experiencing relapsing secondary syphilis was considered to be a "clinical relapse." As far as possible, reinfections were excluded from this last category by means of the following criteria: completion of the prescribed course of treatment; blood negative to all serologic tests on two consecutive observations at least one month apart following completion of treatment; new lesion, not typical of recurrence, appearing prior to a serologic relapse. Spinal fluid test results could not be used in defining the final results as listed, because of the fact that, for several of the treatment methods, such examinations were reported for too small a proportion of the cases.

TABLE 2.—*Methods of Treatment Evaluated in the U. S. P. H. S. Field Study of Massive Arsenotherapy for Syphilis, Number of Cases of Early Syphilis Treated by Each Method, and Number of Cases Followed After Treatment by Each Method*

Method of Treatment	Cases of Early Syphilis Treated	Cases Followed After Treatment
Slow intravenous drip, neoarsphenamine	110	100
Slow intravenous drip, mapharsen	2,451	1,971
Rapid intravenous drip, mapharsen	450	398
Multiple syringe injection, mapharsen	275	228
Multiple syringe injection, mapharsen plus tyhoid vaccine	779	637
Multiple syringe injection, arsphenamine	261	241
Miscellaneous other methods	23	...
Total, all methods	4,351	3,575

TABLE 3.—*Length of Time Cases Were Followed After Treatment and the Time at Which Clinical Relapses Occurred*

Months After Treatment	Cases Treated, Per Cent Still Under Observation	Clinical Relapses: Per Cent Occurring in Period	Clinical Relapses: Cumulative per Cent
1	82.4	1.3	1.3
2	76.7	3.3	4.6
3	70.2	10.2	14.8
4	64.6	13.0	27.8
5	59.9	11.4	39.2
6	55.2	12.3	51.5
7	50.2	11.8	63.3
8	46.1	8.9	72.2
9	42.5	5.0	77.2
10	39.1	5.1	82.3
11	35.9	2.9	85.2
12	33.3	3.0	88.2
13-15	30.7	3.4	91.6
16-18	24.4	3.8	95.4
19-21	19.5	0.8	96.2
22-24	15.5	2.1	98.3
25-30	12.1	0.9	99.2
31-36	7.4	0.4	99.6
37 and over	4.0	0.4	100.0

For each treatment method included in the study, a greater percentage of satisfactory results was obtained among primary cases than among secondary cases. The percentages are given in table 4. Likewise, among patients with secondary syphilis there developed more serologically fast cases, serologic relapses and clinical relapses proportionally than among primary cases. An average of 85.7 per cent satisfactory results was obtained in primary syphilis as opposed to 70.4 per cent in secondary syphilis. Six and four tenths per cent of the primary cases exhibited clinical relapse and 13.1 per cent of the secondary cases.

TABLE 4.—*Results Obtained with Massive Arsenotherapy in Early Syphilis, Showing the Estimated Percentage of Cases in Each Final Outcome Following Each Method of Treatment, by Diagnosis at Time of Treatment*

Method of Treatment	Satisfactory: Primary	Satisfactory: Secondary	Serologically Fast: Primary	Serologically Fast: Secondary	Serologic Relapse: Primary	Serologic Relapse: Secondary	Clinical Relapse: Primary	Clinical Relapse: Secondary
Slow drip, neoarsphenamine	89.5	85.7	5.3	2.4	...	2.4	5.3	9.5
Slow drip, mapharsen	85.7	71.8	4.5	10.6	3.2	3.4	6.6	14.2
Rapid drip, mapharsen	85.4	64.5	5.7	9.9	4.7	9.9	4.2	15.7
Multiple injection, mapharsen	85.4	72.3	2.4	9.2	...	4.0	12.2	14.5
Multiple injection, mapharsen plus typhoid vaccine	88.5	70.2	2.3	17.7	4.6	4.4	4.6	7.7
Multiple injection, arsphenamine	78.6	56.7	3.9	14.2	5.8	8.7	11.7	20.4
Total, all treatments	85.7	70.4	4.3	11.9	3.5	4.6	6.4	13.1

In comparing the several methods of treatment it was found that, although the differences in results from one treatment to another were not great, nevertheless not all of them can be ascribed to chance. In general, excluding the original slow drip with neoarsphenamine, which was found by its authors to be too reactive, the best results were obtained through the use of multiple injections of mapharsen combined with typhoid vaccine. Least effective, both in inducing satisfactory results and in preventing clinical relapses, were multiple injections of arsphenamine. However, when the material was analyzed by amount of arsenical given (table 7) there were indications that the poor results obtained with this method may have been due to insufficient dosage.

TABLE 5.—*Results Obtained with Massive Arsenotherapy in Early Syphilis, Showing the Estimated Percentage of Cases in Each Final Outcome Following Initial Treatment and Following Retreatment*

Stage at Time of Treatment	Final Outcome: Satisfactory	Serologically Fast	Serologic Relapse	Clinical Relapse
Primary syphilis	85.7	4.3	3.5	6.4
Secondary syphilis	70.4	11.9	4.6	13.1
Clinical relapse following routine treatment	59.2	29.5	6.8	4.5
Clinical relapse following massive arsenotherapy	68.9	17.2	4.0	9.9
All clinical relapses	67.2	20.0	4.6	8.2
Possible reinfections, any stage	73.5	17.0	3.8	5.7

The therapeutic results, then, that can be expected from present methods of massive arsenotherapy are at best about 85 to 90 per cent "cure" among cases in which treatment is started in the primary stage of the disease and 70 per cent among cases in which treatment

is started in the secondary stage. Primary cases show about 5 to 6 per cent clinical relapse, and secondary cases from 10 to 13 per cent. Perhaps as grave a consideration as the frequency of clinical relapses is the 8 per cent of primary cases and the 15 to 20 per cent of secondary cases that either remain serologically positive or show a serologic relapse, for any late manifestations of the disease which may occur will probably appear among these cases.

No significant differences were found between the results obtained in original infections and those obtained in reinfections. And, as shown in table 5, while the reinfections showed both a larger percentage of satisfactory results and a smaller percentage of clinical relapses than did the relapses, the differences were not statistically significant. This is probably due to the small number of reinfections. As might be expected, primary syphilis, first infection, gave much better results than did relapses. However, there was no difference in the results obtained among previously untreated secondary infections and those obtained among patients with secondary manifestations occurring as a relapse after treatment, either routine or intensive in type.

In a considerable number of the cases treated by means of slow and rapid drip with mapharsen, blood specimens were examined at the time of treatment by means of the Kahn quantitative test. With both these methods of treatment it was found that cases whose starting titer was 20 units or below had significantly more satisfactory results and fewer relapses than did cases with a starting titer higher than 20 units. These results are given in table 6.

In order to investigate the effect of the amount of arsenical administered, the results following each method of treatment were analyzed at various dosage levels. Table 7 presents the final outcome for each treatment scheme above and below the dosage levels which gave the largest differences. None of the differences are very great, and none are clearly significant. However, in nearly every case the differences are in the direction of better results with larger doses, and, when all treatments are combined, the difference is significant. In every instance more clinical relapses occurred among the smaller dosage groups.

Bismuth was administered in connection with the intensive treatment course in a portion of the cases in which either rapid or slow drip with mapharsen was given. Table 8 shows the results following these two treatments divided according to whether or not bismuth was given. It can be seen that with rapid drip the use of bismuth improved the results decidedly. Among the patients receiving this drug there were 92.4 per cent satisfactory results, compared with 70.4 per cent among those not receiving it. Conversely there were 12.8 per cent of clinical relapses among those not given bismuth and none among those who did get it.

Among the cases treated by slow drip, the results were not so clearcut. When all cases treated by this method were divided only according to whether or not bismuth was given, no significant differences were found. It was noted, however, that bismuth was used more frequently in the treatment of secondary syphilis

TABLE 6.—*Results Obtained with Massive Arsenotherapy in Early Syphilis, Showing the Estimated Percentage of Cases in Each Final Outcome Following Rapid and Slow Drip with Mapharsen by Quantitative Kahn Test Titer at Time of Treatment*

	Satisfactory		Serologically Fast		Serologic Relapse		Clinical Relapse	
Method of Treatment	Titer 20 Units or Less	Titer Over 20 Units	Titer 20 Units or Less	Titer Over 20 Units	Titer 20 Units or Less	Titer Over 20 Units	Titer 20 Units or Less	Titer Over 20 Units
Rapid drip, mapharsen	83.6	69.0	6.0	8.5	4.4	9.0	6.0	13.5
Slow drip, mapharsen	80.2	72.1	4.4	12.0	7.2	3.3	8.2	12.6

TABLE 7.—*Results Obtained with Massive Arsenotherapy in Early Syphilis, Showing the Estimated Percentage of Cases in Each Final Outcome for Each Method of Treatment, by Amount of Arsenical Given*

Method of Treatment and Amount of Arsenical Given	Satisfactory	Serologically Fast	Serologic Relapse	Clinical Relapse
Slow drip, neoarsphenamine				
Less than 4,000 mg.	87.4	6.3	...	6.3
4,000 mg. and over	88.0	4.8	1.2	6.0
Slow drip, mapharsen				
Less than 1,200 mg.	76.9	4.8	1.2	17.1
1,200 mg. and over	75.9	9.7	3.8	10.6
Rapid drip, mapharsen				
Less than 800 mg.	70.6	9.5	9.0	10.9
800 mg. and over	82.3	6.5	4.1	7.1
Multiple injection, mapharsen				
Less than 1,200 mg.	72.4	6.9	4.8	15.9
1,200 mg. and over	74.2	12.9	...	12.9
Multiple injection, mapharsen, plus typhoid vaccine				
Less than 800 mg.	72.0	14.8	5.6	7.6
800 mg. and over	83.0	10.0	...	7.0
Multiple injection, arsphenamine				
Less than 2,400 mg.	59.2	13.2	3.9	23.7
2,400 mg. and over	73.6	9.0	7.1	10.3

TABLE 8.—*Results Obtained with Massive Arsenotherapy in Early Syphilis, Showing the Estimated Percentage of Cases in Each Final Outcome Following Administration of Slow and Rapid Drip With Mapharsen With and Without Bismuth*

	Final Outcome			
Method of Treatment and Administration of Bismuth	Satisfactory	Serologically Fast	Serologic Relapse	Clinical Relapse
Rapid drip, mapharsen				
Bismuth given	92.4	3.8	3.8	....
No bismuth given	70.4	8.4	8.4	12.8
Slow drip, mapharsen				
Bismuth given	72.3	10.9	3.1	13.7
No bismuth given	72.5	8.7	3.7	15.1

TABLE 9.—*Results Obtained with Massive Arsenotherapy in Early Syphilis, Showing the Estimated Percentage of Satisfactory Results and of Clinical Relapses for Each Method of Treatment, by Age at Time of Treatment*

	Per Cent Satisfactory Results		Per Cent Clinical Relapses	
Method of Treatment	Under 25 Years of Age	25 Years of Age and Over	Under 25 Years of Age	25 Years of Age and Over
Slow drip, neoarsphenamine	82.2	90.7	8.9	3.7
Slow drip, mapharsen	73.3	81.3	14.5	8.2
Rapid drip, mapharsen	75.5	76.2	11.4	8.6
Multiple injection, mapharsen	67.3	79.8	18.2	10.6
Multiple injection, mapharsen plus typhoid vaccine	68.6	84.2	9.7	2.7
Multiple injection, arsphenamine	58.4	74.1	23.0	9.5
Total, all methods	71.7	81.1	13.6	7.4

than in primary syphilis and also that among primary cases it was given more frequently to those who were seropositive than to those who were seronegative.

Differences in response to syphilotherapy may be inherent in certain characteristics of the patient population, even though these characteristics are not in any way determined by the disease or its treatment. In seeking to investigate these points the results of intensive therapy were analyzed by race, sex and age.

With regard to age a very definite bias in favor of older patients was found. From table 9 it can be seen that 81.1 per cent of the older group reached a satisfactory outcome as opposed to 71.7 per cent of the younger patients, and whereas only 7.4 per cent of the older patients experienced clinical relapses, 13.6 per cent of the younger ones did. These differences are too large to be ascribed to chance.

TABLE 10.—*Results Obtained with Massive Arsenotherapy in Early Syphilis, Showing the Estimated Percentage of Satisfactory Results Following Each Method of Treatment, by Race and Sex*

	Race		Sex		Race and Sex			
					White		Nonwhite	
Method of Treatment	White	Non-white	♂	♀	♂	♀	♂	♀
Slow drip, neoarsphenamine	91.1	80.6	87.9	....	91.1	....	80.6	....
Slow drip, mapharsen	82.2	70.8	80.7	70.5	88.2	74.7	74.2	66.4
Rapid drip, mapharsen	77.9	74.6	83.8	66.5	86.4	66.7	82.6	66.5
Multiple injections, maphar sen	78.7	70.0	77.2	69.0	77.7	80.7	76.6	62.5
Multiple injections, maphar sen plus typhoid vaccine	84.5	67.5	80.3	64.8	90.1	74.2	73.6	61.0
Multiple injections, arsphenamine	68.2	63.1	64.9	....	68.2	....	63.1	....
Total, all methods	82.1	70.4	80.1	68.5	86.0	74.5	74.6	64.6

TABLE 11.—*Results Obtained with Massive Arsenotherapy in Early Syphilis, Showing the Estimated Percentage of Clinical Relapses Following Each Method of Treatment, by Race and Sex*

	Race		Sex		Race and Sex			
					White		Nonwhite	
Method of Treatment	White	Non-white	♂	♀	♂	♀	♂	♀
Slow drip, neoarsphenamine	1.5	19.4	7.1	....	1.5	....	19.4	....
Slow drip, mapharsen	7.9	15.5	11.5	12.3	5.6	10.7	16.7	13.9
Rapid drip, mapharsen	15.4	8.1	7.1	13.4	10.2	22.2	5.8	10.4
Multiple injections, maphar sen	11.7	15.8	15.7	11.5	15.9	3.2	15.6	16.1
Multiple injections, maphar sen plus typhoid vaccine	3.7	8.9	7.1	7.0	5.0	1.5	8.6	9.2
Multiple injections, arsphenamine	15.9	17.4	16.9	....	15.9	....	17.4	....
Total, all methods	8.1	13.0	10.5	11.3	7.1	10.0	13.6	12.1

From table 10 it can be seen that there are both race and sex differences in the response to rapid treatment for syphilis. The proportion of satisfactory results obtained was consistently higher for the white race than for the nonwhite races and was also higher for males than for females. These differences remain significantly great when the four race-sex groups are considered separately: white males show a greater percentage of satisfactory results than nonwhite males; white females than nonwhite females; white males than white females; nonwhite males than nonwhite females.

The pattern of differences between the races and sexes is not so clearcut when considering the proportion of clinical relapses as it is in the case of satisfactory results. The racial difference is still apparent, but there seems to be no difference between males and females. The clinical relapse rates are shown for race and sex in table 11. The nonwhite races show a significantly greater predisposition toward infectious relapse than does the white race for all treatments combined. From one sex to another, however, neither is there uniformity of direction in the differences from one treatment method to another nor is there a significant difference observable in all treatments combined.

The outstanding conclusion to be drawn from the foregoing analysis by patient population characteristics is that the group most resistant to treatment was that of young nonwhite females.

The present study is primarily concerned with the therapeutic efficacy of massive arsenotherapy, and the detailed analysis of reactions is not yet complete. The only data concerning treatment complications yet compiled are derived from a hand tabulation of the abstracts available on Aug. 1, 1943. At that time a search was made for cases showing evidence of encephalopathy which advanced to the point of convulsions. It was found that for all types of treatment combined there were 3.2 fatal encephalopathic reactions per thousand courses of treatment and 3.9 nonfatal, a total of 7.1 per thousand. No statistically significant differences could be demonstrated between individual clinics, methods of treatment, sexes or age groups. It was noted, however, that encephalopathy occurred more than twice as frequently among white persons as among nonwhites, and also that this type of reaction appeared to be more frequently fatal among white females than among white males or among nonwhites of either sex.

SUMMARY

1. The therapeutic results in a group of 4,351 massive arsenical treatments for syphilis have been studied.

2. It was found that the best results (excluding the highly reactive slow intravenous drip administration of neoarsphenamine) followed the use of multiple syringe injection of mapharsen combined with typhoid vaccine.

3. The most effective massive arsenotherapy yields 85 to 90 per cent of satisfactory results in primary syphilis and 70 per cent in secondary syphilis.

4. About 5 to 6 per cent of the primary cases relapsed and 10 to 13 per cent of the secondary cases.

5. Patients treated when the titer of the Kahn quantitative test on the blood was 20 units or below experienced more frequent satisfactory results and fewer clinical relapses than did cases with a titer greater than 20 units.

6. Results were slightly better among patients receiving larger doses of arsenicals than among those receiving smaller doses.

7. The administration of bismuth during the period of treatment appeared to improve the results obtained.

8. The following differences in response to treatment were noted: Patients over 25 years of age responded better than those under 25; males responded better than females; whites responded better than nonwhites.

9. Least satisfactory results to treatment were obtained among young nonwhite females.

10. Acute encephalopathy was observed in 7.1 per thousand treatments. Of these 3.2 per thousand were fatal and 3.9 per thousand were followed by recovery. No difference could be demonstrated between treatments with regard to the frequency of this type of reaction.

THE INITIAL NEUROLOGIC AND PSYCHIATRIC SYNDROME OF PULMONARY GROWTH

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The syndrome described in this article demonstrates the fact that psychologic and somatic phenomena continually merge into one another, and that in pathology it is impossible to separate them.

It is not widely known that patients with a growth in the thoracic cavity often go in the first place to a neurologist. If one bears in mind that the initial complaint which gives rise to so serious a diagnosis is generally of vague neuralgic pains, it is important to consider the subject closely. The anamnesis is characteristic: the apparently healthy patient complains of spreading pains in the back or limbs. Intermittent neurologic signs and symptoms may be present or not. The patient is psychologically somewhat disturbed; his attention is rather closely fixed on his own pains. His intimates or his family doctor send him to the neurologist with a diagnosis of hysteria or neurosis. In the ordinary way the neurologist gives him psychotherapy. The next stage is the x-ray (in the initial phase this may not reveal anything immediately) and with the determination of the blood sedimentation rate the diagnosis is settled. It is however already possible to diagnose with fair certainty an intrathoracic growth before the x-ray gives a clear picture. If one finds, for example, sharp, spreading pains in the right arm and in the chest whether or not with hyperesthesia and abnormal tendon reflexes, and if at the same time the blood sedimentation rate is very much increased, a negative x-ray should not be relied on.

As a summary the following brief remarks should be added. In the case of my series of 9 patients covering a period of four years, it was not possible for the most part to attempt any pathologic research at the seat of the growth. The x-ray diagnosis and the clinical history as a whole were guaranties of the diagnosis. I saw still more of the same type of patient who had had only one consultation with a general practitioner. My impression is that these neurologic phenomena with an initial growth occur quite frequently—strictly speaking the metastases of intrathoracic tumors in the central nervous system come under the foregoing heading also. The pulmonary growth, especially, tends to produce metastases in the brain.

REPORT OF CASES

CASE 1.—A man aged 69 came for consultation because he had recently suffered from neuralgic pains in the right shoulder blade. His wife found him changed, more discontented and more irritable. His son, a doctor, considered that his father was always too ready to complain of his own ills. The neurologic examination was negative. The patient had not grown thinner. An x-ray examination revealed no abnormality in the spinal column or in the upper part of the lungs. Iontophoretic treatment did not relieve the pain. The patient went on a journey abroad in good spirits; on one occasion during the journey he brought up blood stained mucus, to which no attention was paid. With antineuralgic treatment the condition remained bearable. Six months after the first examination he suddenly brought up a lot of blood. The pain had meanwhile become much worse. The blood sedimentation rate increased, there was anemia, and the x-ray examination of the lungs showed a growth on the right hilus. Three months later the patient died.

CASE 2.—A man aged 57 suffered from spreading pains in the left arm. From time to time he had attacks of choking and of tiredness. He had been treated for neuralgic pains for some time, but latterly he had been more and more depressed, let himself go, became irritable; for this reason he was sent by his family doctor to the neurologist. The pains were usually at night, with a tingling feeling in the left hand. There were no motor or sensory disturbances, nor were there any typical centers of pain, apart from pressure on the ribs on the upper left side. The test for angina pectoris by the doctor was negative. A week later, after preliminary antineuralgic treatment, it appeared that the trachea was slightly displaced toward the right. This put us on the right track. The x-ray examination showed a large growth in the left half of the thorax which presumably issued from the first costal arch and pressed on nearly the whole left lung (sarcoma?). The blood sedimentation rate was 124 mm. Fourteen days later the tumor began to grow outward. In spite of x-ray therapy the patient died four months later.

CASE 3.—A man aged 56 suffered for many years from depression complicated by all kinds of neuralgic pains. As his chronic psychosis deteriorated and he became more violent owing to bitterness against his family, he was placed in a hospital for rest therapy. Examination revealed a slight anemia and a blood sedimentation rate of 60. Profiting by previous experiences and in view of the neuralgic pains in his chest and arms, an x-ray examination was made, with negative results. On these grounds it was decided to give a mild course of barbital, after which the patient felt psychologically much better. After two months he had a relapse, but his condition was still such that he could be nursed at home. Six months later the neuralgic pains were worse; they spread down the right arm and the right side of the thorax. The blood sedimentation rate was now 66. Eight months later came the first hemoptysis. When fresh x-ray films were taken a big pulmonary growth could be seen stretching from the right hilus. Nine months later the pains were more severe, especially at night, waves of pain running through the right hand and arm. There were no neurologic signs. In the tenth month there was slight paralysis in the right hand and arm, with edema of the hand, arm and head. A week later the patient died suddenly in his sleep.

CASE 4.—The patient's illness was announced by apparent sciatic pains, for which he was treated for over six months. The general health was good, but his family complained of his "hysterical" behavior; that is to say, he became more childish, tried to attract attention to his illness and claimed to suffer from more disturbances of functions than was actually the case. On examination a positive symptom of Laségue was found with atrophy of the right calf, but—and this did not belong to the sciatic picture—a Babinski reflex of the soles of the feet and increased reflexes. At first both patient and family set themselves against clinical observation and lumbar puncture; and because the hysteriodepressive syndrome dominated, less attention was paid to neurologic signs. When the patient complained of more pain and neuralgic pains spread to the neck, the family agreed to clinical observation. Here too the x-ray revealed the diagnosis—a large growth at the hilus of the lung, probably growing in the spinal column, while at the third and fourth vertebrae of the neck there was actually a metastasis. The blood picture showed a simple anemia; the blood sedimentation rate was very high (110 after one hour).

CASE 5.—This case is very much akin to the preceding one. It also began with a sciatic syndrome, but it appeared easier to understand as there were metastases in the third, fourth and fifth lumbar from a bronchial carcinoma in the right upper lobe. Here also I was initially called into consultation for psychosis in connection with the sciatic symptoms. The man was childish, negative, depressed. The condition of the patient could not be ameliorated, and the dagnosis was confirmed by clinical examination after the doctor had really convinced the patient that it was necessary. The blood sedimentation point was 91 mm. in the first hour; there was no anemia. This patient also died one and one half months after admission in a state of cachexia.

CASE 6.—Here the diagnosis was more difficult, because the illness began clearly with pains and paralysis of the left arm. The patient was a man aged 67. At the first examination the reflexes in the paralyzed arm were increased, the pupils reacted rather slowly and there were indications of venereal disease in the anamnesis. For these reasons a thorough examination was considered necessary. At the clinical examination, however, no clues on which to base such an enquiry were found; blood and liquor reactions were negative, the x-ray film of the skull was normal, there were no abnormalities in ventricular pressure, blood pressure and renal functions were normal. We were faced with this problem: we had not yet considered the pathologic phenomena which he certainly showed, a blood sedimentation rate of 56 mm. and anemia. In the hospital the patient coughed up blood stained phlegm for the first time. An x-ray film of the lung was then taken and in the left apex of the lung a distinct pressure on the plexus had produced the phenomena already noted. The general condition of the patient remained good for a long time; there were no pathologic developments. A year passed before the patient died.

CASE 7.—A transport worker aged 52 had complained for over a year of rheumatic pains from the left elbow to the neck. The neurologist was consulted as to the possibility of a neuritis in the plexus. From time to time the finger tips were swollen and painful. On admission to the hospital it appeared that he also had pains in the upper part of his chest, and there was a sporadic coughing up of purulent sputum. A year later in another hospital rib section on account of empyema was performed. From the x-ray it appeared that the whole thorax was deeply shadowed and the radiologist suspected multiple tumors. After examination with iodized oil a complete stoppage was found in the left main bronchus at the bifurcation. There was anemia and a blood sedimentation rate of 87 mm. In the sputum there were no tubercle bacilli and no pneumococci, but many streptococci. Electrocardiographic examination was negative. One and a half months after admission to the hospital the patient died after the usual cachectic phenomena had appeared. At the autopsy it appeared that there was a carcinoma spreading from the left lung with metastases in the other lung, pleuritis carcinomatosa, and metastases in both kidneys, along the spinal column and in the liver.

The next 2 patients came to my notice in the confusion and excitement shortly after the German occupation, and for that reason the initial phenomena were all the more difficult to interpret.

CASE 8.—A woman aged 52, who had suffered in the bombardment of Rotterdam, was thereafter depressed and reserved, and five weeks later she came under my care for a sudden attack of asthma and traces of nervousness. She was first treated with sedatives, but after two weeks she had another attack of asthma. This gave rise to the taking of an x-ray film; a tumor of the lung was visible. She had a blood sedimentation rate of 110. The illness lasted six months, the psychosis remaining right up to the last.

CASE 9.—A man aged 44 was thrown against a wall by blast and afterward complained of pains in the shoulder and tingling in the fingers of the right hand. In the same way there was a certain dulness and apathy. The shoulder was x-rayed, but this produced no clues. The psychologic disintegration increased, neurologic symptoms slowly emerged and the reflexes decreased. The blood sedimentation rate was too high, and in view of earlier experiences a diagnosis of intrathoracic tumor was decided on. After six weeks' treatment the patient died very suddenly. He had shown no signs of lung symptoms. At the autopsy a primary lung carcinoma was revealed.

COMMENT

If we analyze the case histories of these people suffering from growths in or near the lung, who in the early stages come to the nerve specialist, we must direct our attention to the following facts:

The Psychologic Symptoms.—The psychiatrist ought to be able to establish the diagnosis of one or another bodily process on the psychologic picture alone. There is unfortunately no typical psychologic process belonging to distinct organic lesions. There are, however, distinct syndromes which fasten suspicion on a bodily origin. Hysterical depression in the presenile period is significant, even before the onset of arteriosclerosis of the central nervous system. Among my 9 patients, in whom there was a certain negativism along with the syndrome, we must ascribe the psychologic symptoms to a toxic disorder of the central nervous system.

The Pain.—The pain was intense in all the cases. It was not only local but was spread over all parts of the body. This is in accordance with the toxic etiology of neuralgia, above all in those cases in which peripheral neurologic signs appeared. Here also factors connected with abnormal pressure on the sympathetic chain must be taken into account. One of my patients experienced the most intense pain a few days before it was clear from the congestion in the arm that there was pressure on the big vessels. In other cases (2 and 4) in which the tumor was already very big and the pain came later, we ought to have been able to establish the position, owing to the pressure on and erosion of the neighboring skeletal parts. The symptom of neuralgic pain pointed at least as often to a general disorder as to a specific involvement of the sensitive nerve tissue.

OTHER INITIAL SYMPTOMS OF GROWTH IN THE LUNG

Most growths in the lungs will show their true character without neurologic and psychologic clues. None of my patients had a growth beginning with hemoptysis, and among a few there was no instance of hemoptysis. It will more often happen that these patients die without any suspicion of pulmonary disease. A man aged 53 whom I saw in the last stages of his illness and who, because of his neurologic symptoms, paralysis of the arm and leg, was thought to be suffering from acute multiple sclerosis, died suddenly with hemoptysis, there being unfortunately no possibility of x-ray examination. In the initial stages also there was no cachexia among my patients. In all these cases there was an increased blood sedimentation rate from the first examination.

SUMMARY

Nine persons suffering from pulmonary growths consulted a psychiatrist and neurologist concerning their initial symptoms. Violent neuralgic pains with a negative hysterical depression and a raised blood sedimentation rate are a characteristic triad of symptoms demanding an immediate radiologic examination of the lungs. The difficulty of diagnosis lies in the initial psychologic interpretation of the symptoms.

Blood Transfusion in Modern Times.—Scientific use of transfusion in modern times may be traced to James Blundell (1790-1877). Having been much agitated over the loss of many patients through uncontrollable puerperal hemorrhage, he first experimented on animals which had seemingly bled to death and were revived by blood taken from animals of the same species. He then proceeded to investigate the possibilities of transfusion in cases of human hemorrhage. It should be noted here that before Blundell experiments were made by means of bladders fastened to quills; hypodermic needles were unknown. Blundell experimented with various instruments and developed in 1818 a syringe with a three way valve.—Gordon, Benjamin Lee: The Romance of Medicine, Philadelphia, F. A. Davis Company, 1944.

Clinical Notes, Suggestions and New Instruments

MYELOPATHY AS A RESULT OF INTENSIVE TREATMENT OF SYPHILIS WITH MAPHARSEN

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It has been observed that intensive treatment of early syphilis with mapharsen by means of multiple injections or intravenous infusion increases the incidence of complications referable to the nervous system. Encephalopathy and neuropathy head the list of injuries to the nervous system from all types of arsenical preparations used in the treatment of syphilis, whereas myelopathy is a rare sequel. Glaser and the Imermans [1] reviewed the literature in 1935 and found 146 reported cases of encephalitis, 8 of myelitis and 4 of encephalomyelitis and added 2 personally observed cases of encephalitis and 1 of encephalomyelitis. Lichtenstein [2] recently reported the pathologic changes in a case of toxic myelopathy which followed the intravenous injection of neoarsphenamine. We are adding the following case to the list of possible complications during intensive treatment of syphilis with mapharsen:

REPORT OF CASE

A. F., a white woman aged 26, was delivered of a normal male infant at the University Hospital in 1936, at which time the serologic reactions on the blood were negative for syphilis. After this pregnancy she developed varicose veins in the right leg and wore an elastic bandage to prevent swelling of the right foot. She was delivered of a normal female infant in 1937; in 1942 in her fifth pregnancy her Wassermann reaction was negative. On the day following the birth of her child Jan. 10, 1944 she developed pustular lesions about the mouth, lesions which gradually spread until practically the entire body was involved. The blood Wassermann reaction on March 6 was positive,

The patient was admitted to the hospital March 7, 1944 with a very unusual, pustuloulcerative type of secondary syphilis of the face, extremities and trunk. The lesions varied from 1.5 to 5 cm. in diameter and were heavily crusted. Removal of the crust revealed a granulating base. Although these areas were quite moist, a positive dark field examination could not be obtained. There were no lesions on the mucous membranes.

The temperature was 99 F. on admission. Her weight was 118 pounds (53.5 Kg.). Her pupils were circular in outline and equal and reacted well to light and in accommodation. Ophthalmoscopy was negative. The other cranial nerves were intact. There was advanced dental caries. Examination of the chest and abdomen, with the exception of the skin, showed nothing remarkable. The blood pressure was 110/80. The right ankle was slightly swollen. The strength and coordination of the extremities were good, the deep reflexes were present and equal, and the sensory examination was negative. The rectal sphincter tone was normal. The urine had a specific gravity of 1.015, was acid in reaction and contained no albumin, blood or sugar. The erythrocyte count was 4,500,000, the leukocyte count 10,650 and the hemoglobin value 11 Gm. The blood smear revealed no abnormalities. The Kolmer, Kahn and Kline reactions on the blood were positive.

The five day treatment of syphilis was started on March 13. After intravenous infusion of 72 mg. of mapharsen a fever of 101.4 F. developed and the treatment was discontinued for that day. The schedule was : March 13, 72 mg. of mapharsen; March 14, 240 mg.; March 15, 240 mg.; March 16, 250 mg.; March 17, 240 mg. and March 18, 180 mg., total 1,222 mg.

Within a few hours after completing this course of treatment she developed a fever of 103 F. She complained of low back pain and weakness and numbness of both lower extremities. The right leg was more severely affected. Within two days she complained of generalized stiffness of the body, inability to void and loss of bowel control; in addition she developed a generalized toxic erythema. The essential neurologic changes were as follows: There was weakness of both lower extremities, but the right side was weaker than the left. The extensors of the right ankle and toes were paralyzed. The abdominal reflexes and the knee jerk reflexes were absent, both achilles jerks were hyperactive and there was an unsustained ankle clonus bilaterally. The response to plantar stimulation was absent on the right and extensor on the left. All types of sensation were reduced to an estimated 10 per cent of normal over the lateral aspect of the right leg and dorsum of the right foot and to an estimated 80 per cent up to the level of the costal margins. The urinary bladder was greatly distended, and rectal sphincter tone practically zero. After a few days of intermittent catheterization an indwelling catheter was installed.

On March 27, nine days after completion of the course of treatment, she developed a fever of 103.4 F., and on the following day her temperature reached 105.6 F. The urine was loaded with leukocytes. A diagnosis of urinary tract infection secondary to neurogenic disease of the bladder was made, and she was placed on sulfathiazole by mouth in addition to large amounts of fluids orally and intravenously. The infection subsided within one week.

Lumbar puncture on April 3 revealed clear fluid which was under an initial pressure of 140 mm. with the patient in the horizontal position. A prompt rise and fall occurred with compression and release of the jugular veins; the fluid contained a trace of globulin (Pandy test), no blood and 4 mononuclear cells per cubic millimeter; the total protein was 54 mg. per hundred cubic centimeters, the colloidal gold curve was 1111100000 and the Wassermann reaction was negative.

The treatment consisted essentially of care of the bladder and physical therapy to the lower extremities. Her course was one of gradual improvement. Cystometrograms, which at first showed a flaccid bladder, began to reveal a gradual return of bladder tone. In a month's time she had regained control over her rectal sphincter and was able to walk a few steps with assistance. At the end of six weeks there was still a toe and ankle drop on the right, the deep reflexes were hyperactive in both lower extremities, and the response to plantar stimulation was still extensor on the left. She was now voiding normally, and there was no residual urine. She was fitted with a short leg brace to support the right leg.

She was discharged from the hospital May 29, approximately ten weeks after her mapharsen therapy. She had numerous scars over the face and other portions of her body as a result of the pustuloulcerative lesions. There was slight improvement in the strength of the dorsiflexors of the right foot. All pyramidal tract signs had disappeared. Sensation was intact except for an estimated response of 75 per cent to light touch and pain over dermatomes fifth lumbar and first sacral on the right.

The Kolmer, Kline and Kahn reactions on the blood remained positive during her stay in the hospital. At no time during her illness did she exhibit signs or symptoms of hemorrhagic encephalitis.

COMMENT

Complications referable to the nervous system occur during all types of arsenotherapy of syphilis, but there is general agreement that rapid treatment increases the frequency of these accidents, which usually involve the brain and peripheral nerves. Opinions vary as to the pathogenesis of a cord lesion of this type. Lichtenstein [2] concluded that the arsphenamines may produce spinal cord changes through vascular alterations resulting in perivascular hemorrhages, or through a combination of various parenchymatous changes with or without vascular phenomena. Moore [3] regards this type of accident as usually due to therapeutic shock involving a previously latent syphilitic endarteritis of the cord vessels, although in certain instances proof is lacking.

CONCLUSIONS

1. This case illustrates an unusual and rare complication of intensive mapharsen therapy.

2. The reaction occurred in the absence of clinical evidence of hemorrhagic encephalopathy.

3. In spite of pronounced bladder, bowel and lower extremity involvement, this patient showed remarkable improvement.

From the Department of Neurology and the Department of Dermatology and Syphilology, State University of Iowa.

1. Glaser, M. A.; Imerman, C. P., and Imerman, S. W.: So-Called Hemorrhagic Encephalitis and Myelitis Secondary to Intravenous Arsphenamines, Am. J. M. Sc. **189**: 64-79 (Jan.) 1935.

2. Lichtenstein, B. W.: Acute and Subacute Toxic Myelopathies Following Therapy with Arsphenamines, Arch. Neurol. & Psychiat. **48**: 740-760 (Nov.) 1942.

3. Moore, J. E.: The Modern Treatment of Syphilis, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1941, p. 113.

Council on Pharmacy and Chemistry

The electron microscope is giving us a new understanding of the physical structure of the microscopic and submicroscopic agents of disease, the bacteria, rickettsias and viruses. It appears that these microparasites may be arranged along a scale of diminishing size and complexity of organization which tends to parallel the scale of their decreasing metabolic independence and increasingly obligatory parasitism.

Simultaneously new insight into the fundamental host-parasite relationships is currently laying the foundation on which a more useful understanding of susceptibility and resistance to these disease agents will be based. Finally the principles and mechanisms underlying the spectacular recent successes in chemotherapy are beginning to assume a clarity which would seem to point the way toward eventual extension of chemotherapy into areas in which it has not as yet been successful.

These rather wide prospects are presented by the chairman of the National Research Council Committee on Applications of the Electron Microscope, who is also a member of this Council.

AUSTIN E. SMITH, M.D., *Secretary.*

PATHOGENIC BACTERIA, RICKETTSIAS AND VIRUSES AS SHOWN BY THE ELECTRON MICROSCOPE

THEIR RELATIONSHIPS TO IMMUNITY AND CHEMOTHERAPY

I. MORPHOLOGY

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AND
THOMAS F. ANDERSON, PH.D.
PHILADELPHIA

Current textbooks, teaching and discussion in bacteriology do not reflect adequate understanding of the structure of the bacterial cell or of the smaller parasitic entities known as rickettsias and viruses. It is a well recognized principle in natural science that understanding of structure is basic to analysis of function. In most areas of the medical sciences this principle is not only accepted as a matter of course but, more important, is expressed in the actual content of these sciences. However, several special circumstances have tended to foster the development of bacteriology without an adequate basis of understanding even of the structure of bacteria. Bacteriology has been pursued primarily for its practical usefulness, only secondarily as a science in its own right; structural details of the bacterial cell are close to, and in many cases beyond, and the structural details of rickettsias and viruses are completely beyond, the limits of resolution of the light microscope; the ordinary staining methods of bacteriology are relatively primitive as compared with the technics of general cytology. All of these circumstances have tended to obscure the fact that there is a morphology of the microparasitic agents of disease, adequate understanding of which will have both theoretical and practical value. The use of bacteria and their components as diagnostic and immunizing agents will be more intelligent and more effective when it is generally understood that the bacterial cell has differentiated parts and when the localization of chemical and antigenic components in the several parts has been learned. Only since the introduction of the electron microscope has it become evident also that rickettsias and the larger viruses also have an essentially cellular morphology.

New possibilities for the study of the structure of bacteria, rickettsias, viruses, phage and of fine structure in tissue have been opened up by the electron microscope.[1] This instrument, by virtue of its greatly increased power of resolution, has increased the useful magnification available for investigation of fine structure by a factor of about sixtyfold as compared with the light microscope, or twentyfold as compared with the best ultraviolet microscope.

REVELATION OF STRUCTURE BY THE ELECTRON MICROSCOPE

Resolution and Image Formation in the Electron Microscope.—The useful magnification provided by any microscope is determined by its power of resolution. Resolution may be defined as the smallest distance by which two particles in the object may be separated and still appear as two particles in the image. This distance, d, has been considered as given by the equation $d = \frac{0.5\lambda}{N.A.}$, in which λ is the wavelength of the radiation used and $N.A.$ the numerical aperture of the lens. For visible light the smallest wavelength that can be used is in the neighborhood of 400 millimicrons (cf. fig. 28) and the smallest theoretically distinguishable distance about 120 millimicrons. In ordinary practice the limit with the light microscope is reached with isolated objects or elements of structure that are less than 250 millimicrons in diameter. Using ultraviolet radiation of wavelength 257 millimicrons and a quartz lens system, Barnard [2] has been able to photograph particles with a diameter of 75 millimicrons. When high velocity electrons ($\lambda = 0.005$ millimicron) are used as the observing medium, the minimal resolvable detail is very much smaller. In actual current practice with objects of biologic interest, resolution of 4 millimicrons is attained with the electron microscope; assuming the resolving power of the unaided human eye to be 0.2 millimeter, this corresponds to a useful magnification of 50,000 diameters. With denser objects resolution of 1.5 millimicrons has been achieved, corresponding to a useful magnification of 130,000 diameters.

The electron microscope [3] is analogous in principle to the light microscope. Each has a source of radiation, condenser lenses for concentrating the radiation onto the specimen, an objective lens which forms an enlarged first image of the specimen and a projection lens which forms the final image [4] (fig. 1). In the electron microscope the source of radiation is a thermionic cathode in an "electron gun." Electrons from this hot cathode are

Owing to lack of space, this article is abbreviated in THE JOURNAL by the omission of twenty-six illustrations. The complete article appears in the authors' reprints.

Dr. Mudd was chairman of the Committee on Applications of the Electron Microscope, National Research Council, 1940-1944. Dr. Anderson was RCA Fellow on the Electron Microscope, National Research Council, 1940-1942.

The privilege of republishing certain of the electron micrographs was extended by the authors and the journals cited in the corresponding references in the bibliography and by the Williams and Wilkins Company, Baltimore. The electron pictures, with a few exceptions, were taken at the RCA Research Laboratories. Many courtesies were extended by Dr. V. K. Zworykin and Mr. James Hillier. The pictures of figures 12, 23, 33, 34 and 35 were taken with an RCA type B electron microscope at the Johnson Foundation for Medical Physics, University of Pennsylvania.

1. Marton, L.: The Electron Microscope in Biology: Annual Review of Biochemistry, Stanford University P. O., Calif., Annual Reviews, Inc. **12**: 587-614, 1943.
2. Topley, W. W. C., and Wilson, G. S.: The Principles of Bacteriology and Immunity, ed. 2, Baltimore, William Wood & Co., 1936, p. 18.
3. Zworykin, V. K.; Hillier, J., and Vance, A. W.: An Electron Microscope for Practical Laboratory Service, Tr. American Institute of Electrical Engineers **60**: 157-161 (April) 1941. Zworykin, V. K., and Hillier, J.: A Compact High Resolving Power Electron Microscope, J. Applied Physics **14**: 658-673 (Dec.) 1943. Zworykin, V. K.; Hillier, J., and Vance, A. W.: Electron Microscope, in Glasser, O.: Medical Physics, Chicago, Year Book Publishers, 1944.
4. Anderson, T. F.: The Study of Colloids with the Electron Microscope, from Advances in Colloid Science, New York, Interscience Publishers, Inc., 1942, vol. 1, pp. 353-390.

accelerated to a high velocity by a high potential difference as soon as they leave the cathode. They are then subjected to a magnetic (or electrostatic) field which acts as a condenser lens and controls the convergence of the electron rays irradiating the specimen. This beam passes through the object, through the magnetic (or electrostatic) objective lens and projector lens, finally to form the image on the fluorescent viewing screen or photographic plate. Electrons which pass through the object undeflected of course contribute to the brightness of the image; any electrons which are sufficiently deflected in the object so that they do not pass through a small aperture in the middle of the objective lens do not contribute to the brightness of the image. The image actually formed, therefore, is essentially a record of the amount of scattering of each electron pencil which traverses the object, and this scattering is to a first approximation proportional to the density times the thickness of matter traversed.

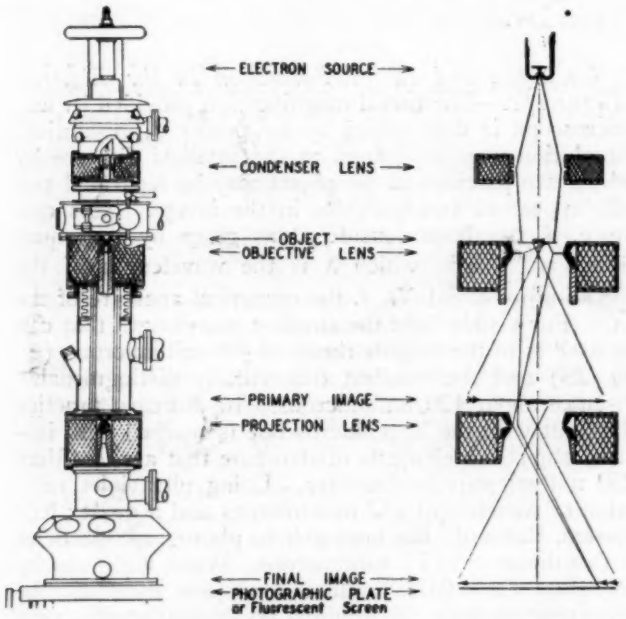

Fig. 1.—The electron microscope. On the left is a scale drawing and on the right a schematic diagram of the instrument showing the arrangement of lenses and the formation of images. (After Anderson,[4] fig. 1.)

Although the mechanism of image formation is different, electron micrographs may therefore be considered as analogous to x-ray pictures, the darkness and brightness depending on the thickness and density of the specimen. Electron pictures resemble x-ray pictures in another important respect, i. e. that the entire thickness of the usual specimen is in focus. The electron micrograph is thus a projection of the total thickness of the field under examination; this lack of a critical focal plane may cause the illusion of two separate objects, one of which overlies the other, appearing as parts of one object in the electron micrograph.

Since air itself scatters electrons, the interior of the electron microscope is kept at a high vacuum. The bacteria or other specimens are mounted, usually unstained, on a thin collodion film. Some shrinkage of parts of the bacterial cell, in particular the fluid or potentially fluid inner protoplasm, frequently occurs, as a result of the unavoidable drying; some distortion of the cell and its parts, due to drying against the mount, may also occur. We have not seen evidence of appreciable alteration of such small objects as bacteria by action of the electron beam itself.

THE STRUCTURE OF THE BACTERIAL CELL AS SHOWN BY THE ELECTRON MICROSCOPE

Bacteria are cells, with structurally differentiated parts. A cell wall, structurally distinct from the inner protoplasm, can be detected in electron pictures of each of the kinds of bacterium thus far adequately studied; this includes most micro-organisms pathogenic for man; cocci and rod forms, both gram positive and gram negative and spiral forms (e. g. figs. 2, 3, 4, 5, 6, 17, 22, 26 and 42). Differentiation within the inner protoplasm can be detected in many species in the form of dense spheroidal (fig. 7) or discoidal (fig. 8) granules or of less well defined areas of greater or lesser density (fig. 9). Spores form within the protoplasm of sporulating species (fig. 10); flagella are demonstrable on motile species. Nucleoprotein demonstrable chemically within the bacterial cell can be seen as localized under certain, but not all, conditions in what has been interpreted as a simple nucleus (fig. 11). Capsules in certain species such as the pneumococcus (fig. 12) and extracellular slime in others, such as Streptococcus pyogenes,[5] are demonstrable outside the bacterial cell wall.

Bacterial Cell Wall and Inner Protoplasm.—The bacterial cell wall is in the solid state; it maintains its shape and position with relatively little alteration under conditions of drying or mechanical injury to the bacterial cell. The inner protoplasm with its limiting surface is either fluid or a gel which readily passes into the sol state, as is evidenced by the frequency with which the protoplasm appears shrunken away from the cell wall in dried specimens and escapes from the cell wall following injury of the bacterial cell. Bacterial cells may be broken by intense sonic vibration. After such treatment many of the cell walls appear as "ghosts" [6] from which the inner protoplasm has escaped (fig. 2), and jagged lines of fracture of the cell wall may be found [7] (fig. 13). Shrinkage or escape of inner protoplasm from the cell wall may be brought about by appropriate chemical reagents [8] (figs. 14, 15 and 16). Intact cells and "ghosts" of autolyzed cells [7] may be found together in preparations particularly from aging cultures (fig. 17).

In bacteria which are not quite completely divided, and in those which form chains, such as Streptococcus pyogenes (fig. 18) or clusters such as Staphylococcus aureus (fig. 19), the bacterial cell walls can be seen to be continuous from cell to cell; a connecting strand of protoplasm may or may not be present between the adjacent cells according to the completeness and nature of the cell division.

Differentiations Detectable Within the Protoplasm.—The inner protoplasm itself may appear homogeneous in electron pictures. Or inhomogeneities may be apparent in the inner protoplasm, as in micrographs of strains of Fusobacterium,[9] Treponema pallidum (fig. 7), Mycobacterium tuberculosis [10] (fig. 21), Corynebac-

5. Marton, L.: The Electron Microscope: A New Tool for Bacteriological Research, J. Bact. **41**: 397-413 (March) 1941, figure 6.

6. Mudd, S., and Lackman, D. B.: Bacterial Morphology as Shown by the Electron Microscope: I. Structural Differentiation Within the Streptococcal Cell, J. Bact. **41**: 415-420 (March) 1941.

7. Mudd, S.; Polevitzky, K.; Anderson, T. F., and Chambers, L. A.: Bacterial Morphology as Shown by the Electron Microscope: II. The Bacterial Cell Wall in the Genus Bacillus, J. Bact. **42**: 251-264 (Aug.) 1941.

8. Morton, H. E., and Anderson, T. F.: The Morphology of Leptospira Icterohemorrhagiae and L. Canicola as Revealed by the Electron Microscope, J. Bact. **45**: 143-146 (Feb.) 1943. Mudd and Anderson.[38]

9. Mudd, S.; Polevitzky, K.; Anderson, T. F., and Kast, C. C.: Bacterial Morphology as Shown by the Electron Microscope: III. Cell Wall and Protoplasm in a Strain of Fusobacterium, J. Bact. **44**: 361-366 (Sept.) 1942.

10. Mudd, S.; Polevitzky, K., and Anderson, T. F.: Bacterial Morphology as Shown by the Electron Microscope: IV. Structural Differentiation Within the Bacterial Protoplasm, Arch. Path. **34**: 199-207 (July) 1942.

terium diphtheriae [11] (fig. 8) and others. These inhomogeneities in the inner protoplasm may be of several kinds. In Fusobacterium (fig. 20), for instance, certain areas of the protoplasm may be denser than other areas,[9] and such characteristic differences may even be apparent in stained preparations [12] viewed with the light

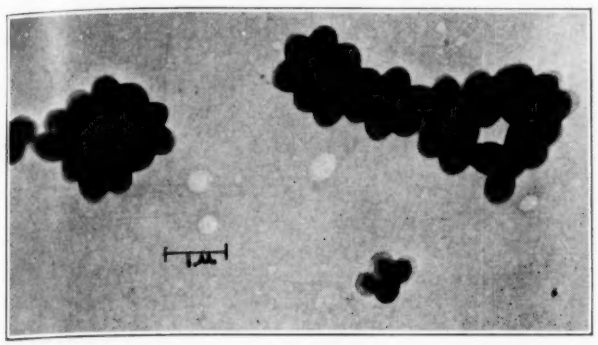

Fig. 3.—Staphylococcus aureus. The light appearing cell walls are particularly clearly shown surrounding the dark inner protoplasm of three of the central cluster of four cells. Reduced from an electron micrograph with a magnification of 10,000 diameters.

microscope. In other species definite spheroidal or discoidal granules of high density may be seen within the protoplasm; such granules have been recorded notably with Mycobacterium tuberculosis (fig. 21), Treponema pallidum (fig. 7), Corynebacterium diphtheriae (fig. 8) and Staphylococcus flavocyaneus [13] (fig. 11). The significance of these granules is not clear in most species. In Staphylococcus flavocyaneus, however, microchemical and cytologic evidence [13] strongly suggests the interpretation of these protoplasmic granules as simple nuclei; it seems probable that a similar interpretation may become appropriate for protoplasmic granules in other species, but this question had best be left open at the present, pending further evidence.

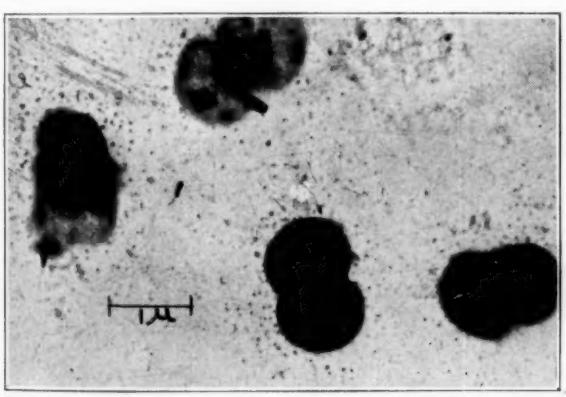

Fig. 4.—Neisseria gonorrhoeae. Two diplococcus pairs are intact; one pair is cytolized. Magnification 11,000 diameters. Reproduced through courtesy of Dr. H. E. Morton.

Inhomogeneities in the bacterial protoplasm may also be produced as artefacts due to coagulation, drying or partial cytolysis, as is of course obvious. Such artefacts are more easily produced in the inner protoplasm than in the cell wall, because of the greater fluidity of the protoplasm. Knaysi [14] has demonstrated that in ordinary bacteriologic specimens (viewed with the light microscope) it is only the inner protoplasm and its limiting membrane which are stained and visible. The cell wall is unstained and invisible unless prepared by special mordant and staining technic. Cell wall and protoplast with protoplasmic membrane are shown particularly clearly in figure 22.[15]

The Capsule.—The pneumococcus capsule has been demonstrated in electron micrographs [16] (fig. 12) as a gel of low density outside of and closely enveloping the cell wall, the cell wall in turn enveloping the bacterial protoplasm with its outer limiting membrane. In the specific capsular swelling reaction the interstices of this capsule are permeated by rabbit immune serum; increase in the thickness and density of the capsule results [17] (figs. 23 and 24).

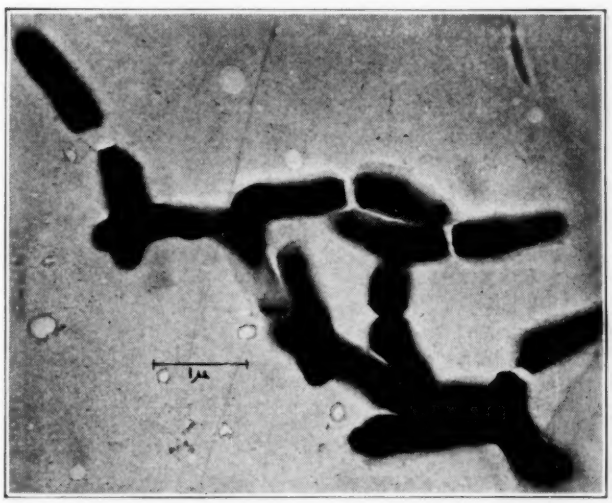

Fig. 8.—Corynebacterium diphtheriae. Discoidal dense granules can be seen near ends of the cells. The protoplasm is shrunken away from the cell walls of several cells. Reduced from an electron micrograph with a magnification of 26,500 diameters. Courtesy of Dr. H. E. Morton.

Flagella.—Flagella are beautifully shown in electron micrographs of motile bacterial species without the necessity of using any mordant or stain. These flagella may occur singly, as on cells of Vibrio cholerae [18] (figs. 14, 15 and 16), may occur all around the bacterial cell, as is the case with Eberthella typhosa [19] (fig. 25) or Clostridium tetani (figs. 17, 26 and 27), or may occur in tufts, as is the case on cells of Treponema pallidum (figs. 6, 7 and 28). Treponema

11. Morton, H. E., and Anderson, T. F.: Electron Microscopic Studies of Biological Reactions: I. Reduction of Potassium Tellurite by Corynebacterium Diphtheriae, Proc. Soc. Exper. Biol. & Med. **46:** 272-276 (Feb.) 1941.

12. Varney, P. L.: The Serological Classification of Fusiform Bacilli, J. Bact. **13:** 275-314 (April) 1927. Hine, M. K., and Bury, G. P.: Morphological and Cultural Studies of the Genus Fusiformis, ibid. **34:** 517-533 (Nov.) 1937.

13. Knaysi, G., and Mudd, S.: The Internal Structure of Certain Bacteria as Revealed by the Electron Microscope: A Contribution to the Study of the Bacterial Nucleus, J. Bact. **45:** 349-359 (April) 1943.

14. Knaysi, G.: Cytology of Bacteria, Botan. Rev. **4:** 83-112 (Feb.) 1938; Observations on the Cell Division of Some Yeasts and Bacteria, J. Bact. **41:** 141-154 (Feb.) 1941; Elements of Bacterial Cytology, Ithaca, N. Y., Comstock Publishing Company, 1944.

15. Johnson, F. H.: Observations on the Electron Microscopy of B. Cereus and Tyrothricin Action, J. Bact. **47:** 551-557 (June) 1944.

16. Mudd, S.; Heinmets, F., and Anderson, T. F.: Bacterial Morphology as Shown by the Electron Microscope: VI. Capsule, Cell Wall and Inner Protoplasm of Pneumococcus Type III, J. Bact. **46:** 205-211 (Aug.) 1943.

17. Mudd, S.; Heinmets, F., and Anderson, T. F.: The Pneumococcal Capsular Swelling Reaction, Studied with the Aid of the Electron Microscope, J. Exper. Med. **78:** 327-332 (Nov.) 1943. Johnson, F. H., and Dennison, W. L.: The Volume Change Accompanying the Quellung Reaction of Pneumococci, J. Immunol. **48:** 317-323 (May) 1944.

18. Mudd, S., and Anderson, T. F.: Selective "Staining" for Electron Micrography: The Effects of Heavy Metal Salts on Individual Bacterial Cells, J. Exper. Med. **76:** 103-108 (July) 1942.

19. The flagella of Eberthella typhosa are undoubtedly peritrichate. However, Pijper (Microcinematography of the Agglutination of Typhoid Bacilli, J. Bact. **42:** 395-409 [Sept.] 1941) has shown that in locomotion the flagella of each typhoid bacillus are plaited together to form a corkscrew shaped "tail," which is the actual locomotor organ.

pallidum was described as without flagella until flagella were demonstrated in electron micrographs.[20]

Spores and Sporelike Bodies.—Spores form within the protoplasm of the cells of bacteria of the genus Clostridium (the tetanus gas gangrene group) and of the genus Bacillus,[7] which includes Bacillus anthracis. In young cultures the protoplasm of the bacterial cells may appear homogeneous (fig. 26). In older cultures much of the protoplasm appears to be condensed into the spores (figs. 10 and 27), which appear as exceedingly dense bodies within a protoplasm of reduced density. Subsequently the spore-mother cell shrivels up (fig. 29) and the spore is freed (fig. 30).

Electron micrographs [21] of Treponema pallidum in a number of instances have shown minute bodies of high density attached to the spirochetal cells (figs. 31 and 32); these dense bodies may be closely applied to the sides of the spirochetes or may be attached to the side of the spirochetal cell by short stalks or may be found free. These bodies have been described by a long series

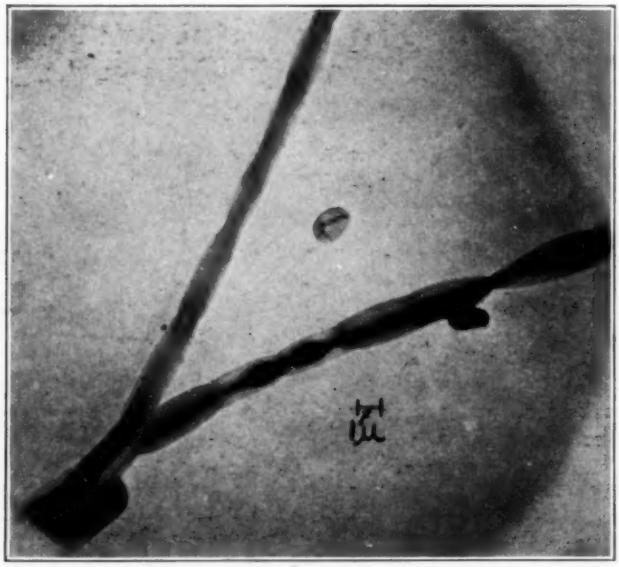

Fig. 10.—Bacillus anthracis. Two chains of vegetative cells; spores appear to be forming in three cells of the lower chain; one extracellular spore is seen from the lower chain. Slightly reduced from an electron micrograph with a magnification of 3,340 diameters.

of investigators; the terms applied to them, "knospen" or "buds" (Meirowsky), "sporelike spherical bodies" (Noguchi), "granules spirochétogènes" (Manouélian), express the interpretation often explicitly made that these are asexual resting or resistant bodies like spores capable of reproducing asexually the normal spirochetal cell. The very impressive accumulation of evidence supporting this interpretation has been reviewed by Meirowsky [22] and Ingraham [23] and more recently by Manouélian.[24] If this interpretation is correct, it might aid, as Ingraham has pointed out, in explaining puzzling aspects of latency, drug resistance and recurrence in syphilis.

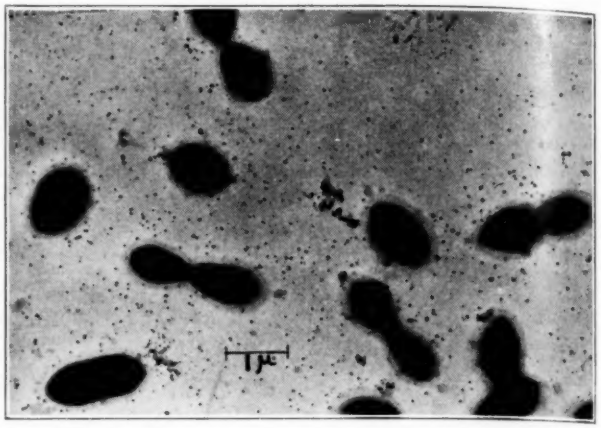

Fig. 12.—Pneumococcus type III. Reproduced from Mudd, Heinmets and Anderson [17] (fig. 1). The delicate areola about each cell or diplococcus pair is the capsule. Reduced from an electron micrograph with a magnification of 11,000 diameters.

It is of interest to consider whether the structural differentiations thus far revealed by the electron microscope afford a clue to the nature of the organization

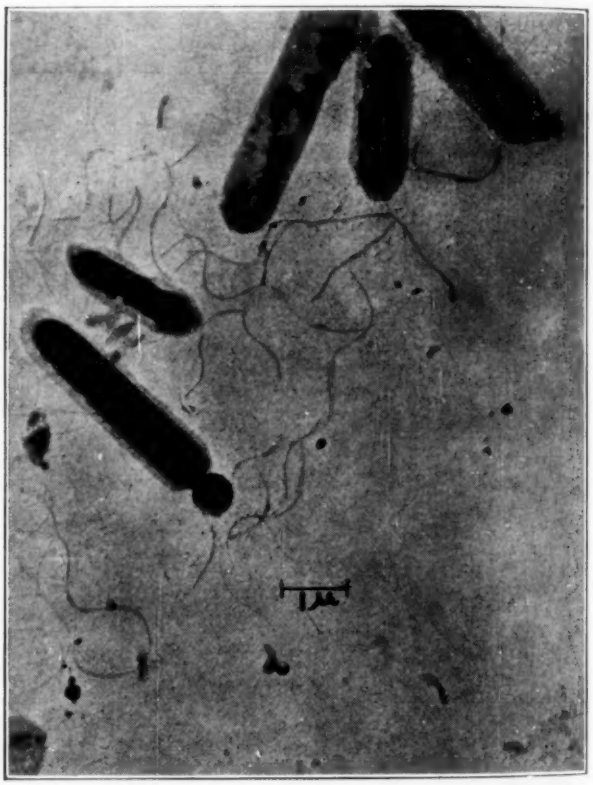

Fig. 17.—Clostridium tetani, 10 day old culture. One intact cell is undergoing unequal division to produce a coccoid cell. The other cells are more or less cytolized. Slightly reduced from an electron micrograph with a magnification of 9,300 diameters.

underlying the amazingly diverse and intricate chemical processes which occur within the minute dimensions of the bacterial cell. Streptococcus pyogenes, for

20. Wile, U. J., and Kearney, E. B.: The Morphology of Treponema Pallidum in the Electron Microscope: Demonstration of Flagella, J. A. M. A. **122:** 167-168 (May 15) 1943. Mudd, S.; Polevitzky, K., and Anderson, T. F.: Bacterial Morphology as Shown by the Electron Microscope: V. Treponema Pallidum, T. Macrodentium and T. Microdentium, J. Bact. **46:** 15-24 (July) 1943; footnote 10. Wile, Pickard and Kearny,[21] Morton and Anderson.[21]

21. Wile, U. J.; Picard, R. G., and Kearny, E. B.: The Morphology of Spirochaeta Pallida in the Electron Microscope, J. A. M. A. **119:** 880-881 (July 11) 1942. Morton, H. E., and Anderson, T. F.: Some Morphologic Features of the Nichols Strain of Treponema Pallidum as Revealed by the Electron Microscope, Am. J. Syph., Gonor. & Ven. Dis. **26:** 565-573 (Sept.) 1942. Mudd, Polevitzky and Anderson.[20]

22. Meirowsky, E.: Spirochaeta pallida, Schaudinn, nebst Bemerkungen über den Entwicklungskreis der Spirochäten, München. med. Wchnschr. **77:** 429-430 (March) 1930.

23. Ingraham, N. R., Jr.: The Life History of the Treponema Pallidum: A Critical Review of the Literature, Am. J. Syph. **16:** 155-189 (April) 1932.

24. Manouélian, Y.: Etude morphologique de Spirochaeta pallida: modes de division; spirochétogène syphilitique, Ann. Inst. Pasteur **64:** 439-455 (May) 1940.

instance, elaborates a characteristic type specific protein, M, whose locus is at least in part at the surface of the streptococcus cell wall;[25] the majority of strains thus far analyzed[26] possess a second type specific agglutinogen T of unknown chemical composition; strains of Streptococcus pyogenes elaborate a carbohydrate C characteristic of the serologic group,[27] protein or nucleoprotein components which cross-react with proteins of streptococci of other groups and of pneumococci[28] and nucleic acids of both the d-ribose and desoxyribose types.[29] Streptococcus pyogenes, given the necessary growth accessories and amino acids,[30] elaborates the enzyme systems required for aerobic and anaerobic respiration. Streptococcus pyogenes in its mucoid phase secretes an extracellular mucoid material, hyaluronic acid,[31] which appears to be identical with a polysaccharide of the mammalian umbilical cord, the vitreous humor[32] and an interfibrillar substance of the corium. Streptococcus pyogenes produces at least three demonstrably distinct physiologically active metabolites which are antigenic: the erythrogenic or skin toxin,[33] the streptococcus hemolysin[34] (streptolysin) and fibrinolysin,[35] which, acting conjointly with a lytic agent in human serum,[36] causes lysis of human and rabbit fibrin. Certain strains at least of Streptococcus pyogenes elaborate an enzyme, hyaluronidase, capable of depolymerizing and hydrolysing hyaluronic acid;[37] this hyaluronidase is known as a "spreading factor" because of its action in facilitating the dissemination of foreign material, doubtless including bacteria and their products, in the corium.[38] S. pyogenes liberates a "lethal agent"[39] of small molecular size.

25. Lancefield, R. C.: Studies on the Antigenic Composition of Group A Hemolytic Streptococci: I. Effects of Proteolytic Enzymes on Streptococcal Cells, J. Exper. Med. **78:** 465-476 (Dec.) 1943.

26. Lancefield, R. C.: Type Specific Antigens M and T of Matt and Glossy Variants of Group A Hemolytic Streptococci, J. Exper. Med. **71:** 521-537 (April) 1940. Lancefield, R. C., and Stewart, W. A.: Studies on the Antigenic Composition of Group A Hemolytic Streptococci: II. The Occurrence of Strains in a Given Type Containing M but no T Antigen, ibid. **79:** 79-88 (Jan.) 1944.

27. Lancefield, R. C.: A Serological Differentiation of Human and Other Groups of Hemolytic Streptococci, J. Exper. Med. **57:** 571-595 (April) 1933. Zittle, C. A., and Harris, T. N.: The Antigenic Structure of Hemolytic Streptococci of Lancefield Group A: X. The Purification and Certain Properties of the Group Specific Polysaccharide, J. Biol. Chem. **142:** 823-833 (Feb.) 1942.

28. Lancefield, R. C.: The Antigenic Complex of Streptococcus Hemolyticus: II. Chemical and Immunological Properties of the Protein Fractions, J. Exper. Med. **47:** 469-480 (March) 1928. Mudd, S., and Wiener, M.: The Antigenic Structure of Hemolytic Streptococci of Lancefield Group A.: XI. Relationships of the Nucleoproteins of Some Species of Streptococci and Pneumococci, J. Immunol. **45:** 21-28 (Sept.) 1942.

29. Sevag, M. G.; Smolens, J., and Lackman, D. B.: The Nucleic Acid Content and Distribution in Streptococcus Pyogenes, J. Biol. Chem. **134:** 523-529 (July) 1940.

30. Bernheimer, A. W., and Pappenheimer, A. M., Jr.: Factors Necessary for Massive Growth of Group A Hemolytic Streptococcus, J. Bact. **43:** 481-494 (April) 1942. Bernheimer, A. W.; Gillman, W.; Hottle, G. A., and Pappenheimer, A. M., Jr.: An Improved Medium for the Cultivation of Hemolytic Streptococcus, ibid. **43:** 495-498 (April) 1942.

31. Kendall, F. E.; Heidelberger, M., and Dawson, M. H.: A Serologically Inactive Polysaccharide Elaborated by Mucoid Strains of Group A Hemolytic Streptococcus, J. Biol. Chem. **118:** 61-69 (March) 1937. Kass, E. H., and Seastone, C. V.: The Role of the Mucoid Polysaccharide (Hyaluronic Acid) in the Virulence of Group A Hemolytic Streptococci, J. Exper. Med. **79:** 319-330 (March) 1944.

32. Meyer, K.; Dubos, R., and Smyth, E. M.: The Hydrolysis of the Polysaccharide Acids of Vitreous Humor, of Umbilical Cord and of Streptococcus by the Autolytic Enzyme of Pneumococcus, J. Biol. Chem. **118:** 71-78 (March) 1937.

33. Dick, G. F., and Dick, Gladys H.: A Skin Test for Susceptibility to Scarlet Fever, J. A. M. A. **82:** 265-266 (Jan. 26) 1924. Dochez, A. R., and Sherman, L.: The Significance of Streptococcus Hemolyticus in Scarlet Fever, ibid. **82:** 542-544 (Feb. 16) 1924. Hottle, G. A., and Pappenheimer, A. M., Jr.: A Quantitative Study of the Scarlet Fever Toxin-Antitoxin Flocculation Reaction, J. Exper. Med. **74:** 545-556 (Dec.) 1941.

34. Smytne, C. V., and Harris, T. N.: Some Properties of a Hemolysin Produced by Group A β-Hemolytic Streptococci, J. Immunol. **38:** 283-300 (April) 1940.

35. Tillett, W. S., and Garner, R. L.: The Fibrinolytic Activity of Hemolytic Streptococci, J. Exper. Med. **58:** 485-502 (Oct.) 1933.

36. Milstone, H.: A Factor in Normal Human Blood Which Participates in Streptococcal Fibrinolysis, J. Immunol. **42:** 109-116 (Oct.) 1941.

37. Meyer, K.; Chaffee, E.; Hobby, G. L., and Dawson, M. H.: Hyaluronidases of Bacterial and Animal Origin, J. Exper. Med. **73:** 309-328 (March) 1941.

38. Chain, E., and Duthie, E. S.: Identity of Hyaluronidase and Spreading Factor, Brit. J. Exper. Path. **21:** 324-338 (Dec.) 1940. McClean, D.: The Capsulation of Streptococci and Its Relation to Diffusion Factor (Hyaluronidase), J. Path. & Bact. **53:** 13-27 (July) 1941.

(Footnotes continued in the next column)

The minute streptococcus cell therefore achieves chemical syntheses which cannot be duplicated in the best equipped chemical laboratories in existence. The concurrent and orderly occurrence of so many chemical

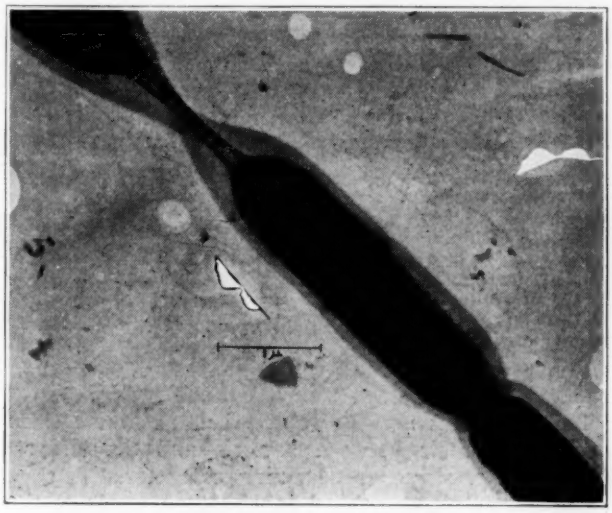

Fig. 22.—Bacillus cereus. Reproduced from Johnson.[15] A "transparent" cell wall encloses the dense inner protoplasm. The cells in early division are joined by a relatively broad band of protoplasm; the cells in more advanced division are connected by a delicate strand of protoplasm (plasmodesmid). Reduced from an electron micrograph with a magnification of 40,000 diameters.

processes within minute dimensions must presuppose some pattern of organization of materials even though this organization is on a molecular scale. It must be admitted that the structural differentiations thus far revealed seem gross and crude in comparison to the

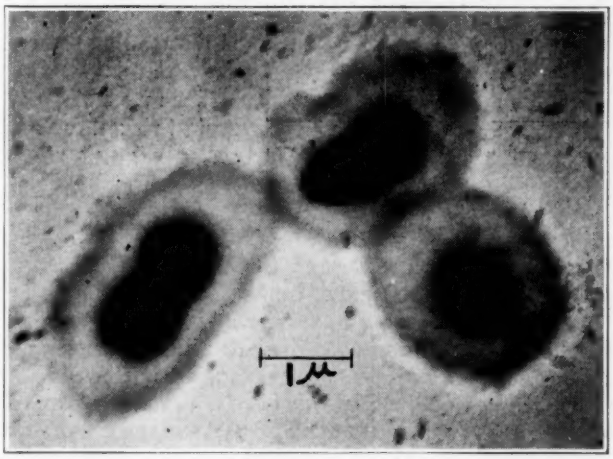

Fig. 23.—Pneumococcus type 1. Reproduced from Mudd, Heinmets and Anderson[17] (fig. 14). Pneumococcus capsule swollen by exposure for three minutes to diluted rabbit antiserum containing specific antibody. Slightly reduced from an electron micrograph with a magnification of 14,000 diameters.

intricate ultramicroscopic organization which one must suppose to exist as a physical basis for the functioning even of bacterial cells. Possibly the discovery of "heavy particles" of complex composition in S. pyogenes by Sevag, Smolens and Stern[40] (see also Stern[41]) or of

39. Harris, T. N.: A Lethal Agent Produced by the Hemolytic Streptococcus, J. Bact. **43:** 739-748 (June) 1942.

40. Sevag, M. G.; Smolens, J., and Stern, K. G.: Isolation and Properties of Pigmented Heavy Particles from Streptococcus Pyogenes, J. Biol. Chem. **139:** 925-941 (June) 1941.

41. Stern, K. G.: Studies on Macromolecular Particles Endowed with Specific Biological Activity, from Frontiers in Cytochemistry, Biological Symposia **10:** 291-321, Lancaster, Pa., 1943.

the minute structural units in the protoplasm of phage lysed E. coli cells by Luria, Delbrück and Anderson [42] or of the thixotropic gel-like organization of the axoplasm of nerve cells of the squid by Richards, Steinback and Anderson [43] may afford first glimmers of light as to what the nature of this pattern of organization may ultimately prove to be.

THE MORPHOLOGY OF RICKETTSIAS AND PLEUROPNEUMONIA-LIKE MICRO-ORGANISMS

Epidemic and endemic typhus fevers, the spotted fevers, Q fever and scrub typhus or tsutsugamushi disease are caused by pathogenic rickettsias. These are [44] "small, often pleomorphic, gram negative, bacterium-like organisms, living and multiplying in arthropod tissues, behaving as obligate intracellular parasites, and staining lightly with aniline dyes." Rickettsia prowazeki, the causal agent of typhus, in its most characteristic form appears as a minute diplobacillus, each member of the diploid form averaging about 0.6 by 0.3 micron.

The rickettsias may be regarded as intermediate in the biologic scale between bacteria and the viruses. Thus in size, shape and staining characteristics they are like little pleomorphic bacteria; they resemble the viruses in their obligate intracellular parasitism. They may also "be regarded as intermediate in their degree of adaption to intracellular conditions, since they grow best in cells which are metabolizing slowly." For a fuller discussion the reader is referred to the review of Pinkerton.[44]

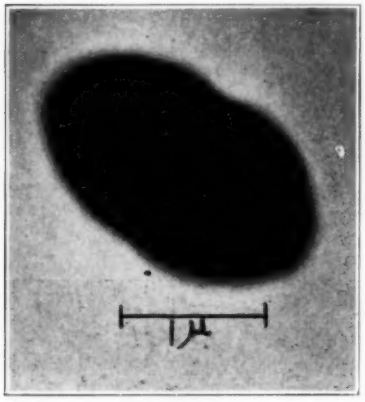

Fig. 24.—Pneumococcus type I treated for thirty seconds with undiluted homologous rabbit antiserum; more advanced stage of swelling than in figure 23. Magnification 19,200 diameters.

The morphology of typical rickettsias has recently been studied and beautifully illustrated with electron micrographs by Plotz, Smadel, Anderson and Chambers.[45] The essential findings have been confirmed by Weiss.[46] These electron pictures show that rickettsias (figs. 33, 34 and 35), like bacteria, are cells with a limiting cell wall clearly distinct from the inner protoplasm. The protoplasm of the rickettsial cells itself shows pronounced differences in density; the denser areas may be more or less sharply localized. Rickettsial cells are pleomorphic, i. e. the cells of a given preparation differ much in size and shape.

Another category of parasitic micro-organisms whose characteristics may be considered as intermediate between bacteria and viruses is the pleuropneumonia-like group. The literature has been reviewed by Sabin.[47] Electron micrographs of the pleomorphic cells of a pleuropneumonia-like strain from arthritis in a rat are recorded by Weiss.[48]

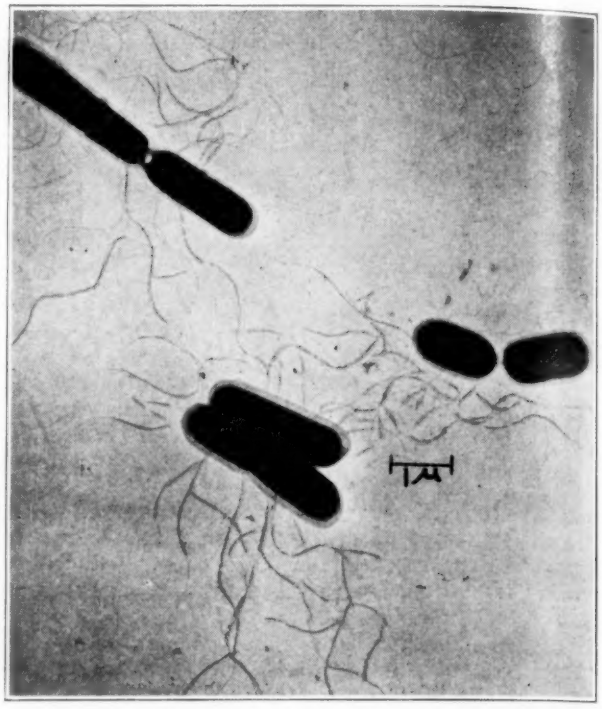

Fig. 26.—Clostridium tetani cells from twenty-four hour culture. In the cells of this young culture the protoplasm is homogeneous within its clear cell walls; stages of cell division and peritrichous flagella are shown. Slightly reduced from an electron micrograph with a magnification of 9,300 diameters.

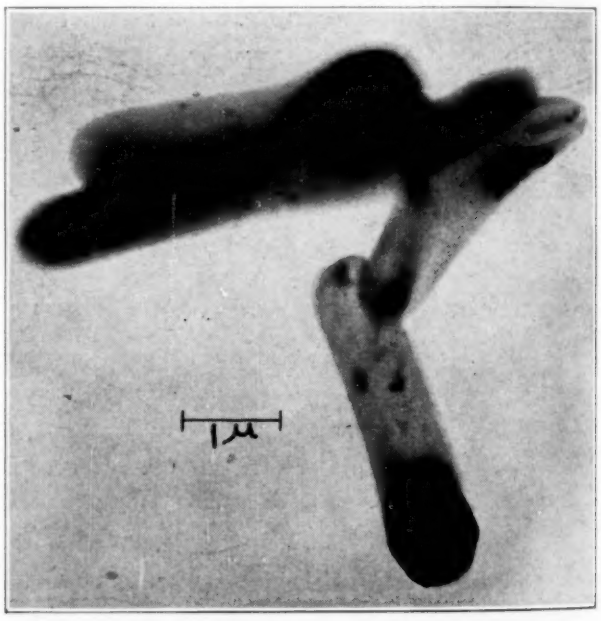

Fig. 27.—Clostridium tetani cells from a three day culture. Terminal "drumstick" spores formed within the bacterial cells. Slightly reduced from an electron micrograph with a magnification of 14,000 diameters.

Highly pleomorphic strains of pathogenic bacteria, which exhibit growth phases resembling pleuropneumonia-like micro-organisms, are currently described by

42. Luria, S. E.; Delbrück, M., and Anderson, T. F.: Electron Microscope Studies of Bacterial Viruses, J. Bact. **46:** 57-77 (July) 1943.
43. Richards, A. G., Jr.; Steinback, H. B., and Anderson, T. F.: Electron Microscope Studies of Squid Giant Nerve Axoplasm, J. Cell. & Comp. Physiol. **21:** 129-143 (April) 1943.
44. Pinkerton, H.: The Pathogenic Rickettsiae, with Particular Reference to Their Nature, Biologic Properties and Classification, Bact. Rev. **6:** 37-78 (March) 1942.
45. Plotz, H.; Smadel, J. E.; Anderson, T. F., and Chambers, L. A.: Morphological Structure of Rickettsiae, J. Exper. Med. **77:** 355-358 (April) 1943.
46. Weiss, L. J.: Electron Micrographs of Rickettsiae of Typhus Fever, J. Immunol. **47:** 353-357 (Nov.) 1943.
47. Sabin, A. B.: The Filtrable Micro-Organisms of the Pleuropneumonia Group, Bact. Rev. **5:** 1-66 (March) 1941.
48. Weiss, L. J.: Electron Micrographs of Pleuropneumonia-like Organisms, J. Bact. **47:** 523-533 (June) 1944.

Dienes and Smith [48a] and by Hesselbrock and Foshay.[48b] Although these forms may depart widely in structure and reproductive behavior from ordinary monomorphic conceptions of bacterial morphology, their organization is still essentially cellular. A pleomorphic strain of Bacteroides funduliformis is under electron microscopic study.[48c]

MORPHOLOGY OF VIRUSES

The viruses are intracellular agents of disease which can be propagated only in the presence of cells that they parasitize. The viral infectious units, moreover, are too small to be resolved and in most cases even to be made visible by ordinary light. It has been natural therefore for many to suppose that viruses are essentially similar to one another in their physical and chemical nature. Other students of viruses, however, notably T. M. Rivers,[49] have for some years advanced reasons for concluding that viruses are heterogeneous and differ widely in nature among themselves. The electron microscope is providing clear morphologic evidence of the heterogeneity of viruses. Vaccinia elementary bodies,[50] as an example of the larger viruses,

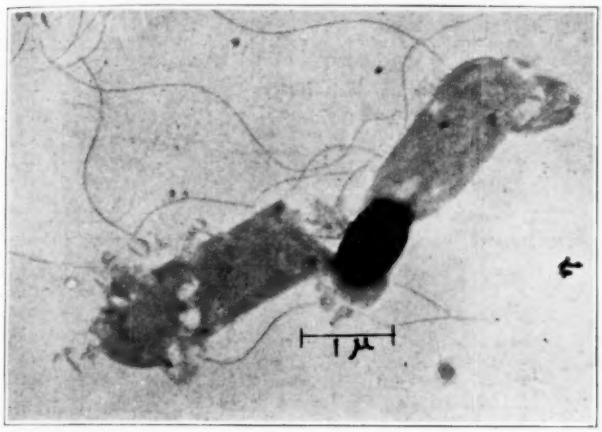

Fig. 29.—Clostridium sporogenes cells from a three day culture. Nothing remains of the vegetative cells except "ghosts," to which peritrichous flagella remain attached; in one "ghost" is a spore. Slightly reduced from an electron micrograph with a magnification of 14,000 diameters.

have an essentially cellular organization resembling that of bacteria; viruses of intermediate size such as bacteriophage still possess structural differentiation;[42] the smallest viruses apparently are giant molecules or minute crystals. A scale of dimensions is given in figure 37.

Animal Viruses.—The morphology of that category of viruses in which the elementary infectious units are largest, namely the psittacosis-lymphogranuloma trachoma group, has not yet been investigated with the electron microscope as far as we are aware. Such studies would be most desirable.

Vaccinia Elementary Bodies.—The morphology of the virus of vaccinia has been presented in clearest detail by Green, Anderson and Smadel,[51] from whom the following is quoted:

48a. Dienes, L., and Smith, W. E.: The Significance of Pleomorphism in Bacteroides Strains, J. Bact. **48:** 125-153 (Aug.) 1944.

48b. Hesselbrock, W., and Foshay, L.: The Morphology of Bacterium Tularense, J. Bact., to be published. Foshay, L., and Hesselbrock, W.: Some Observations on the Filtrability of Bacterium Tularense, J. Bact., to be published.

48c. Smith, W. E., and Mudd, S.: To be published.

49. Rivers, T. M.: Viruses and Virus Diseases (Lane Medical Lectures), Stanford University, Calif., Stanford University Press, 1939.

50. Rivers, T. M.: Virus Diseases, with Particular Reference to Vaccinia, from Virus Diseases, by Members of the Rockefeller Institute for Medical Research, Ithaca, N. Y., Cornell University Press, 1943, pp. 3-31.

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Elementary bodies of vaccinia when viewed by electron microscopy present a high degree of regularity of external outline and of internal form. The particles are almost rectangular in shape and usually possess five circumscribed areas

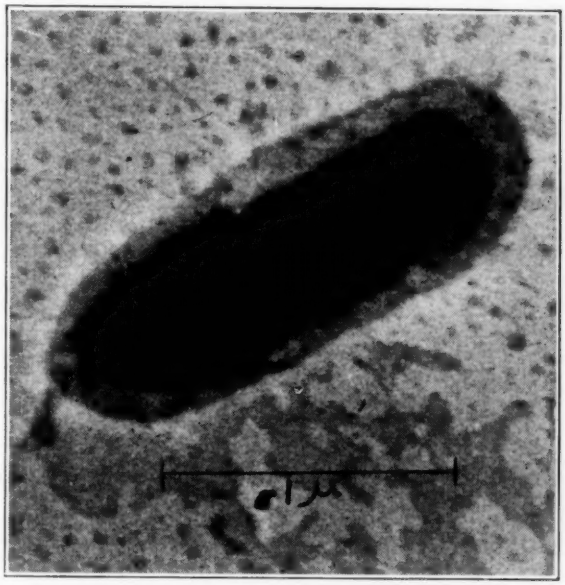

Fig. 33.—Rickettsia prowazeki from epidemic typhus. Reproduced through the courtesy of Dr. Leslie A. Chambers, Johnson Foundation for Medical Physics, University of Pennsylvania. Magnification 40,000 diameters.

which are more dense than the surrounding substance and hence appear darker in the electron micrograph. The central area of condensation in the elementary body is slightly larger than the others which are spread around it; their general arrangement suggests that of the five spots on dice.

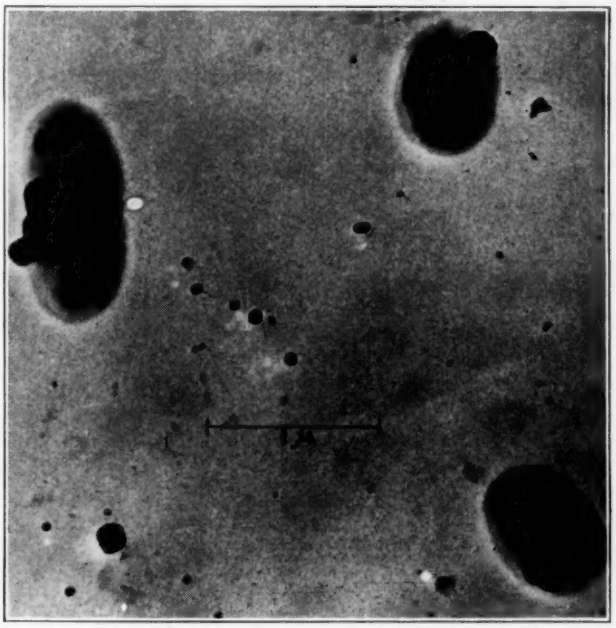

Fig. 34.—Rickettsia prowazeki from murine typhus. Reproduced through the courtesy of Dr. L. A. Chambers. Reduced from an electron micrograph with a magnification of 40,000 diameters.

Elementary bodies which are joined by a narrow bridge of material of lighter density than the bodies themselves are not infrequently encountered. The general shape of the virus particles seems to resemble a brick (fig. 36).

51. Green, R. H.; Anderson, T. F., and Smadel, J. E.: Morphological Structure of the Virus of Vaccinia, J. Exper. Med. **75:** 651-656 (June) 1942.

The elementary bodies may be cytolyzed by ten minutes' exposure to tenth normal sodium hydroxide. The limiting membranes of the elementary bodies remain after cytolysis as "ghosts." "Certain of the ghosts formed in this manner have ruptured; some have wedge shaped gaps in their surfaces and others show substance streaming from them."

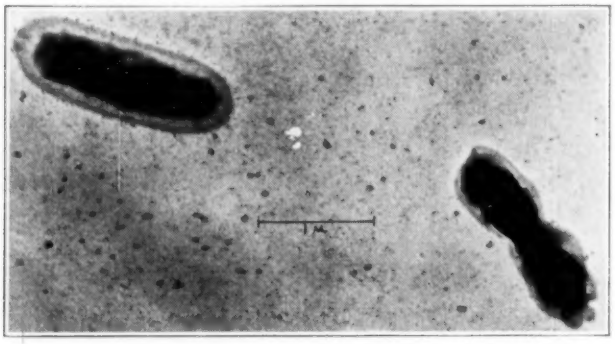

Fig. 35.—Rickettsia (Dermacentroxenus rickettsi) from Rocky Mountain spotted fever. Reproduced through the courtesy of Dr. L. A. Chambers. Reduced from an electron micrograph with a magnification of 40,000 diameters.

Elementary bodies of vaccinia thus resemble bacteria in having an essentially cellular organization. In their complex chemical and antigenic composition [50] they also resemble bacteria.

Influenza, Equine Encephalomyelitis, Papilloma and Foot and Mouth Disease Virus Particles.—Identification and characterization of the elementary infectious units causing virus diseases in man and animals has been rendered very difficult by the fact that until recently the sole sources of such virus particles have been suspensions prepared from infected somatic tissues. Introduction of the method of propagation of virus in the chorioallantoic sac [52] of the embryonated hen's egg with recovery of virus from the chorioallantoic fluid has ameliorated but not removed this difficulty of distinguishing with certainty between infectious agent, tissue detritus and other noninfectious material.[53]

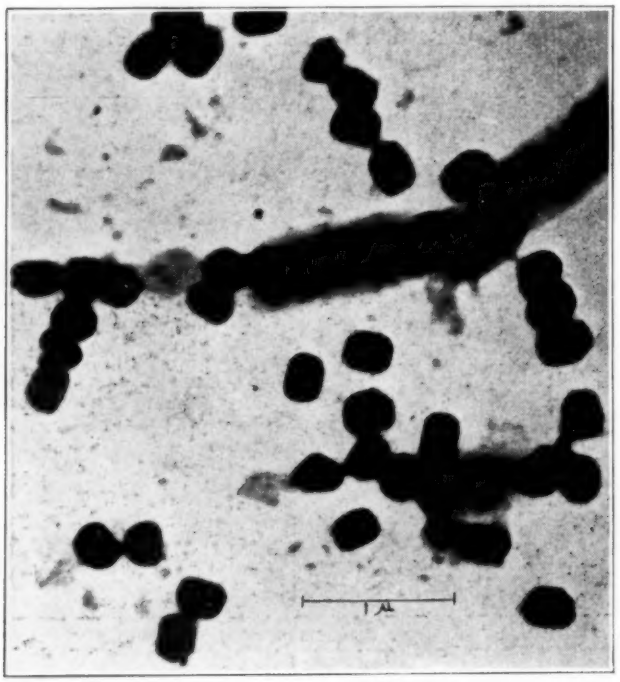

Fig. 36.—Vaccinia elementary bodies. Reproduced through the courtesy of Drs. R. H. Green, T. F. Anderson and J. E. Smadel.[51] The polyhedral bodies are often joined to form diploids or short chains by the continuity of their limiting surface. Reduced from an electron micrograph with a magnification of 45,000 diameters.

Moreover, the physical methods employed for separation of viruses, such as ultrafiltration, ultracentrifugation, electrophoresis and diffusion measurements, are complex and contain possibilities of error which may be incompletely explored. It is not surprising, then, that the morphology of very few viruses of human and other animal diseases may as yet be described without reservation.

COMPARATIVE SIZES OF VIRUSES

	Molecular weight X 10^{-6} (Particle weight X 6.06×10^{-24})	Diam or length X width in mμ
Red blood cells*	173 000 000	7 500
Bacillus prodigiosus*	173 000	750
Rickettsia*	11 100	300
Psittacosis*	8 500	275
Vaccinia*	4 300	225
Myxoma*	4 300	
Canary pox*	4 300	
Pleuro-pneumonia organism*	1 400	150
Pseudo rabies	1 400	
Ectromelia	1 400	
Herpes simplex	1 400	
Rabies fixe*	800	125
Borna disease	800	
Influenza	400	100
Vesicular stomatitis	400	
Staphylococcus bacteriophage†	300	90
Fowl plague	300	
C_{16} bacteriophage	173	75
Chicken tumor I*	142	70
Tobacco mosaic*	35	280 X 15
Cucumber mosaics 3 and 4*	35	
Gene (Muller's est of max size)*	33	125 X 20
Latent mosaic of potato*	26	430 X 9.8
Rabbit papilloma (Shope)*	25	40
Equine encephalitis	23	38
Megatherium bacteriophage	23	
Rift valley fever	11	30
Tomato bushy stunt*	8	26
Hemocyanin molecule (Busycon)*	6.7	22
Yellow fever	4.3	22
Tobacco ring spot*	3.4	19
Louping ill	2.8	19
Hemocyanin molecule (Octopus)*	2.8	20
Alfalfa mosaic*	2.1	16.5
Poliomyelitis	0.7	12
Staphylococcus bacteriophage†	0.4	10
Foot-and-mouth disease	0.4	
Hemoglobin molecule (Horse)*	0.069	15 X 3
Egg albumin molecule*	0.040	9 X 3

Fig. 37.—Comparative sizes of viruses, revised as of June 1944 by W. M. Stanley [73] (fig. 6).

Early studies of the infectious agent of influenza derived from lung tissue led to the conclusion that the diameter of the infectious unit was between 80 and 120 millimicrons. The nature of influenza virus was

52. Woodruff, A. M., and Goodpasture, E. W.: The Susceptibility of the Chorioallantoic Membrane of Chick Embryos to Infection with the Fowl Pox Virus, Am. J. Path. **7**: 209-222 (May) 1931. Scott, J. P.: Swine Influenza, 13th International Veterinary Congress, Zurich-Interlaken **1**: 479-490, 1938. Henle, W., and Chambers, L. A.: The Serological Activity of Extraembryonic Fluids of Chick Infected with Virus of Influenza A, Proc. Soc. Exper. Biol. & Med. **46**: 713-717 (April) 1941. Burnet, F. M.: Growth of Influenza Virus in the Allantoic Cavity of the Chick Embryo, Australian J. Exper. Biol. & M. Sc. **19**: 291-295 (Dec.) 1941. Nigg, C.; Wilson, D. E., and Crowley, J. H.: Studies on the Cultivation of Influenza Virus, Am. J. Hyg., Sect. B **34**: 138-147 (Nov.) 1941.

53. A word of caution is perhaps in order with respect to virus strains propagated within the chorioallantoic sac. Burnet and Bull (Changes in Influenza Virus Associated with Adaptation to Passage in Chick Embryos, Australian J. Exper. Biol. & M. Sc. **21**: 55-69 [June] 1943) have shown that the virus of influenza A, isolated from human cases, on propagation in ovo undergoes phase variation. The adapted or derivative (D) phase differs appreciably in a number of respects from the original (O) phase. Only the derivative phase can be propagated in the allantoic cavity.

reinvestigated by Chambers and Henle [54] and by Chambers, Henle, Lauffer and Anderson,[55] using both suspensions from influenzal lungs and suspensions of virus obtained from the allantoic fluid of chick embryos infected with influenzal virus. The results of sedimentation experiments in the angle ultracentrifuge, together with other observations, seemed to indicate the elementary infectious particles of influenza to be only about 11 millimicrons in diameter. Subsequent work, however, revealed an unreckoned complication dependent on convection currents in the angle centrifuge.[56] Critical reinvestigations of the infectious units of human influenza viruses A and B by Taylor, Sharp and their collaborators,[57] by Stanley [58] and by Friedewald and Pickels [59] have recently indicated in each case that the unit infectious particles of human influenza virus have diameters within the range originally estimated. Similar findings are obtained by Taylor, Sharp, McLean, the Beards, Dingle and Feller [59a] for the virus of swine influenza.

Electron micrographs recently made in the RCA laboratories in Princeton of preparations of PR 8 strain (type A) and Lee strain (type B) human influenza virus, purified and concentrated from infectious extra-embryonic fluids of chick embryos by means of differential centrifugation, are shown in figures 38 and 39. These may be characterized as spheres with a diameter of about 100 millimicrons. Recent analysis by Knight [59b] in Stanley's laboratory indicates, however, that even these infectious purified virus particles have measurable amounts of normal chick components associated with them, possibly adsorbed to their surfaces.

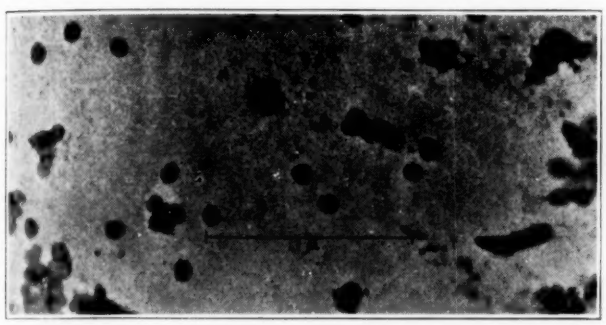

Fig. 38.—Virus of human influenza type A. PR 8 strain. Reproduced through the courtesy of Dr. Wendell M. Stanley. Reduced from an electron micrograph with a magnification of 30,000 diameters.

Infectious particles have recently been separated by Taylor and his collaborators [60] from the tissue of chick embryos infected with the virus of equine encephalomyelitis (eastern strain). These particles are described by the authors as containing 54 per cent fat solvent extractable material, 4 per cent carbohydrate and the remainder nucleoprotein of the ribose type. Electron micrographs show these particles to be of considerable uniformity; they are described by the authors as "probably spherical in shape, constituted peripherally of a substance the limits of which are ill defined in the micrographs in the absence of special treatment." The centers of these particles appear to be denser than the peripheries. After appropriate treatment with isotonic solution of three chlorides diluted 1:3 with 0.25 per cent calcium chloride the peripheral portion of the particles becomes darker and sharper. The authors give the mean diameter of the particles of vague outline as 40.2 millimicrons, that of the particles after treatment with calcium chloride as 47.5 millimicrons.

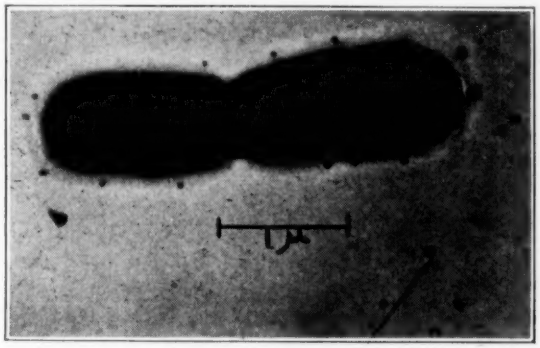

Fig. 42.—Bacteriophage particles, α strain, attached to cells of Escherichia coli. Reduced from an electron micrograph with a magnification of 17,500 diameters.

It may be considered that the observations summarized suggest a differentiation of these virus infectious units into a surface material enclosing an inner material of different composition. If all the foregoing observations are confirmed and the particles are proved

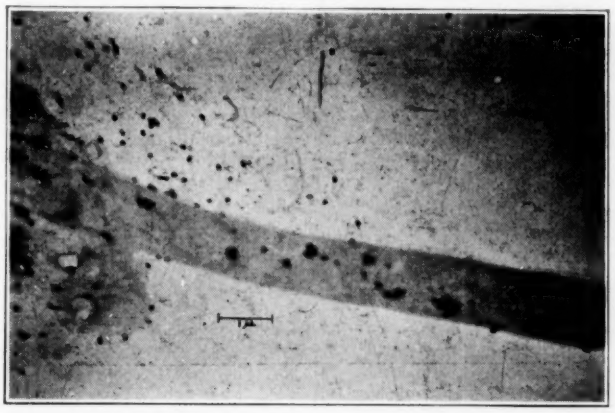

Fig. 43.—Escherichia coli plus virus γ; twenty-three minutes' contact. A bacterium immediately after lysis showing protoplasmic granules and several hundred particles of virus. Reproduced from Luria, Delbrück and Anderson [42] (fig. 5). Reduced from an electron micrograph with a magnification of 20,000 diameters.

54. Chambers, L. A., and Henle, W.: Studies on the Nature of the Virus of Influenza: I. The Dispersion of the Virus of Influenza A in Tissue Emulsions and in Extraembryonic Fluids of the Chick, J. Exper. Med. **77:** 251-264 (March) 1943.

55. Chambers, L. A.; Henle, W.; Lauffer, M. A., and Anderson, T. F.: Studies on the Nature of the Virus of Influenza: II. The Size of the Infectious Unit in Influenza A, J. Exper. Med. **77:** 265-276 (March) 1943.

56. Friedewald, W. F., and Pickels, E. G.: Size of Infective Particle and Hemagglutinin of Influenza Virus as Determined by Centrifugal Analysis, Proc. Soc. Exper. Biol. & Med. **52:** 261-262 (March) 1943.

57. Taylor, A. R.; Sharp, D. G.; Beard, D.; Beard, J. W.; Dingle, J. H., and Feller, A. E.: Isolation and Characterization of Influenza A Virus (PR 8 Strain), J. Immunol. **47:** 261-282 (Sept.) 1943. Sharp, D. G.; Taylor, A. R.; McLean, I. W., Jr.; Beard, D.; Beard, J. W.; Feller, A. E., and Dingle, J. H.: Isolation and Characterization of Influenza Virus B (Lee Strain), ibid. **48:** 129-153 (Feb.) 1944. Sharp, D. G.; Taylor, A. R.; McLean, I. W., Jr.; Beard D., and Beard, J. W.: Density and Size of Influenza Virus A (PR 8 Strain) in Solution, Science **100:** 151-153 (Aug. 18) 1944.

58. Stanley, W. M.: An Evaluation of Methods for the Concentration and Purification of Influenza Virus, J. Exper. Med. **79:** 255-266 (March) 1944. Stanley, W. M.: The Size of Influenza Virus, J. Exper. Med. **79:** 267-283 (March) 1944.

59. Friedewald, W. F., and Pickels, E. G.: Centrifugation and Ultrafiltration Studies on Allantoic Fluid Preparations of Influenza Virus, J. Exper. Med. **79:** 301-317 (March) 1944.

59a. Taylor, A. R.; Sharp, D. G.; McLean, I. W., Jr.; Beard, D.; Beard, J. W.; Dingle, J. H., and Feller, A. E.: Purification and Character of the Swine Influenza Virus, J. Immunol. **48:** 361-379 (June) 1944.

59b. Knight, C. A.: A Sedimentable Component of Allantoic Fluid and Its Relationship to Influenza Viruses, J. Exper. Med. **80:** 83-100 (Aug.) 1944.

60. Taylor, A. R.; Sharp, D. G.; Beard, D., and Beard, J. W.: Isolation and Properties of the Equine Encephalomyelitis Virus (Eastern Strain), J. Infect. Dis. **72:** 31-41 (Jan.-Feb.) 1943; Electron Micrography of the Eastern Strain Equine Encephalomyelitis Virus, Proc. Soc. Exper. Biol. & Med. **51:** 332-334 (Dec.) 1942.

beyond question to be actual infectious units of the virus, it would appear that these and similar virus units may represent the simplest organization [61] of life thus far described.

Electron micrographs of similar character have been published by the same authors [62] for the virus of the

Fig. 45.—Virus of cucumber mosaic 4. Reproduced from Stanley and Anderson [75] (fig. 15). Reduced from an electron micrograph with a magnification of 20,000 diameters.

western strain of equine encephalomyelitis. The authors conclude that "the western strain equine encephalomyelitis virus is a spherical or disk shaped particle of

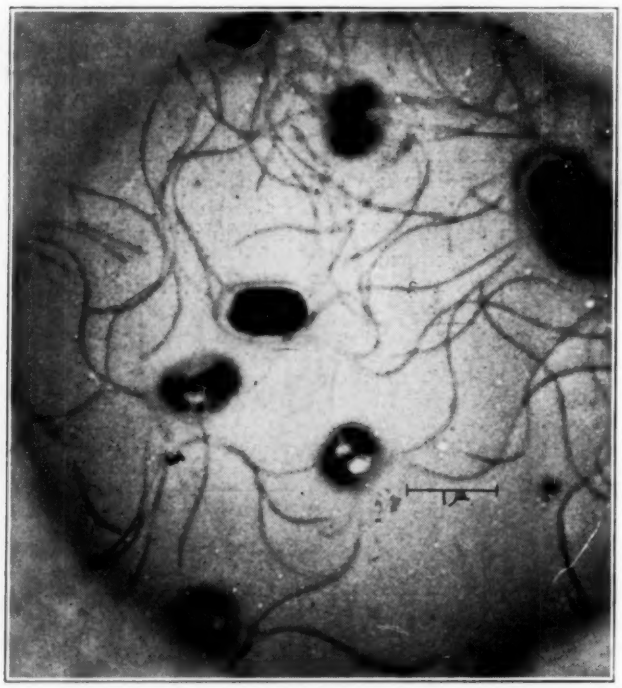

Fig. 47.—Eberthella typhosa sensitized with 1:4 antityphoid rabbit serum; thirty seconds' contact with serum. The flagella are thickened and darkened by deposition of antibody globulin on their surfaces; the bacterial cell walls also have a film of protein from the specific antiserum. Clear spaces due to shrinkage of the inner protoplasm on drying separate the protoplasmic membrane from the serum-sensitized cell walls. Reduced from an electron micrograph with a magnification of 27,000 diameters.

approximately 40 millimicrons in diameter. Electron micrographic images reveal an internal structure characterized by a round or oval region of relatively high density surrounded by an enveloping material of less density." The same authors have reported similar findings for the virus of rabbit papillomatosis.[63]

Glaser and Stanley [64] have separated purified nucleoprotein particles from the blood of silkworms diseased with silkworm jaundice. Electron micrographs and ultracentrifugation data show these particles to be spheres with a diameter of the order of 10 millimicrons and molecular weight of about 300,000. Preparations of these purified particles reproduce the disease in very high dilution; despite this and other suggestive evidence, the authors refrain from drawing the conclusion that these particles are to be considered with certainty as being the active disease agent.

Electron micrographs of particles believed by the authors to be the virus of foot and mouth disease have been published by von Ardenne and Pyl.[65]

Bacterial Viruses.—The physical nature of bacterial viruses (bacteriophage particles) until the introduction of the electron microscope could only be inferred from

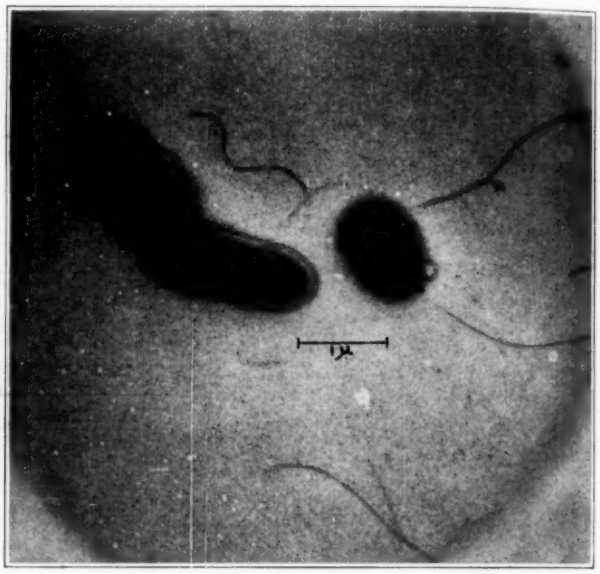

Fig. 48.—Eberthella typhosa sensitized with 1:8 antityphoid rabbit serum; one hundred and five seconds' contact with serum. Flagella and cell somatic surfaces are coated with protein from the specific antiserum. Reduced from an electron micrograph with a magnification of 27,000 diameters.

studies by indirect methods. Investigations prior to 1941 have been reviewed by Krueger and Scribner.[66] Investigations of bacterial viruses with the aid of the electron microscope have been published by Ruska,[67] Kausche and Pfankuch,[68] Luria and Anderson,[69] Luria, Delbrück and Anderson [42] and by Baylor, Severens and Clark.[70]

61. By "organization," in the sense used, is meant differentiation and localization of components of structure which are not merely structural units or "building stones" of a single molecule.

62. Sharp, D. G.; Taylor, A. R.; Beard, D., and Beard, J. W.: Electron Micrography of the Western Strain Equine Encephalomyelitis Virus, Proc. Soc. Exper. Biol. & Med. **51:** 206-207 (Nov.) 1942.

63. Sharp, D. G.; Taylor, A. R.; Beard, D., and Beard, J. W.: Study of the Papilloma Virus Protein with the Electron Microscope, Proc. Soc. Exper. Biol. & Med. **50:** 205-207 (June) 1942.

64. Glaser, R. W., and Stanley, W. M.: Biochemical Studies on the Virus and the Inclusion Bodies of Silkworm Jaundice, J. Exper. Med. **77:** 451-466 (May) 1943.

65. von Ardenne, M., and Pyl, G.: Versuche zur Abbildung des Maul- und Klauenseuche-Virus mit dem Universal-Elektronenmikroskop, Naturwissenschaften **28:** 531-532 (Aug. 16) 1940.

66. Krueger, A. P., and Scribner, E. Jane: The Bacteriophage, Its Nature and Its Therapeutic Use, J. A. M. A. **116:** 2160-2167 (May 10), 2269-2277 (May 17) 1941.

67. Ruska, H.: Die Sichtbarmachung der Bakteriophagen Lyse im Uebermikroskop, Naturwissenschaften **28:** 45 (Jan.) 1940.

68. Kausche, G. A., and Pfankuch, E.: Isolierung und übermikroskopische Abbildung eines Bakteriophagen, Naturwissenschaften **28:** 46 (Jan.) 1940.

69. Luria, S. E., and Anderson, T. F.: The Identification and Characterization of Bacteriophages with the Electron Microscope, Proc. Nat. Acad. Sc. **28:** 127-130 (April) 1942.

70. Baylor, M. R. B.; Severens, J. M., and Clark, G. L.: Electron Microscope Studies of the Bacteriophage of Salmonella Pullorum, J. Bact. **47:** 277-282 (March) 1944.

The definitive studies of phage structure thus far are those of Luria, Delbrück and Anderson.[42] These concern particularly two strains of coli phage, α and γ, which are propagated on the same strain of E. coli; the same bacteria then produce particles of type α if acted on by virus α, and particles of type γ if acted on by virus γ. Both types of phage particle, amazingly, prove to be structurally differentiated "sperm shaped" bodies.

"The particles of virus α have a round head, 45 to 50 millimicrons in diameter and uniformly dark in the micrographs; that means uniformly scattering for 60 kilovolt electrons (fig. 40). To this round head is attached a tail about 150 millimicrons long and not more than 10 to 15 millimicrons thick. The tail appears either straight or slightly curved.

"The particles of virus γ present a very peculiar aspect (fig. 41). To an oval head, 65 by 80 millimicrons, a straight tail, 120 millimicrons long and 20 millimicrons thick, is attached at one of the narrow poles. The head always shows a structure consisting of light and dark areas. The structure, although striking enough to make the particles immediately recognizable, is quite variable. Four frequent configurations can be described schematically as X shaped, Z shaped, inverted Z shaped and diplococcus shaped."

The authors believe that the dark parts represent regions of greater thickness in the dried particle. "It is possible that the particles in the native state are oval, but on drying the more aqueous parts collapse, while the solid parts retain more scattering material, which forms the dark areas of the heads."

Particles of another coli virus are round, 50 to 60 millimicrons in diameter, and no tail can be seen.[42] Particles of a staphylococcus virus have a head about 100 millimicrons in diameter and a tail about 200 millimicrons long.[42]

In later work Anderson [71] has demonstrated that the heads of coliphage particles may be injured by sonic vibration or by ultraviolet irradiation, so as to permit escape of the dense material of the head, leaving its surrounding membrane as a "ghost" to which the tail is still attached.

Plant Viruses.—W. M. Stanley in 1935 announced the preparation of the virus causing mosaic disease in tobacco plants in the form of a crystalline nucleoprotein. Subsequent work has confirmed and greatly extended this discovery. The unit particle of this virus is now well established to be a rod shaped nucleoprotein "macromolecule" whose diameter is about 15 millimicrons and whose length is about 280 millimicrons. These molecules tend to aggregate end to end and side to side to form crystal-like structures of two dimensional regularity (fig. 44). Analysis by x-ray diffraction [72] has shown that the unit particles or molecules of the tobacco mosaic virus nucleoprotein themselves have a definite internal architecture that is due to regular and periodic arrangement of the structural units of which the macromolecule is composed.

Minute amounts of these crystalline macromolecules properly inoculated into susceptible plants of many species are infective; the virus is capable of indefinite propagation in diseased plants; modifications of the virus have been observed to occur in certain host plants and the variant virus strains have been shown to have demonstrable chemical differences from the parent strain.[73] Tobacco mosaic virus thus posseses the properties of reproduction and adaptation, two attributes which have heretofore been considered as distinctively characteristic of living systems; whether or not a crystalline nucleoprotein molecule can be considered to be alive, however, raises questions which cannot profitably be considered here.

Other plant viruses, such as the cucumber mosaic virus (fig. 45), have been shown to be essentially similar to that of tobacco mosaic disease. The virus of tomato bushy stunt (fig. 46),[74] on the other hand, has been shown to consist of spherical particles about 26 millimicrons in diameter and that of tobacco necrosis [75] of essentially spherical particles about 20 millimicrons in diameter.

NOTE.—The second instalment of this paper, by Dr. Mudd, will appear in next week's issue of THE JOURNAL.

71. Anderson, T. F.: The Effect of Sonic Vibration, Ultraviolet Light and *in* on the Bacteriophage Virus, Report to 1st Annual Meeting of Electron Microscope Society of America, New York, Jan. 14, 1944.
72. Bernal, J. D., and Fankuchen, I.: X-Ray and Crystallographic Studies of Plant Virus Preparations, J. Gen. Physiol. **25**: 111-165 (Sept.) 1941.
73. Stanley, W. M.: Chemical Structure and the Mutation of Viruses, in Virus Diseases, Ithaca, N. Y., Cornell University Press, 1943.
74. Stanley, W. M., and Anderson, T. F.: Electron Micrographs of Protein Molecules, J. Biol. Chem. **146**: 25-30 (Nov.) 1942; footnote 75.
75. Stanley, W. M., and Anderson, T. F.: A Study of Purified Viruses with the Electron Microscope, J. Biol. Chem. **139**: 325-338 (May) 1941.

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

AUSTIN E. SMITH, M.D., *Secretary.*

ISO-PAR.—A mixture of water insoluble isoparaffinic acids partially neutralized with hydroxybenzyl-dialiphatic amines. The water insoluble isoparaffinic acids are obtained by oxidation of petroleum hydrocarbons by the passage of a current of oxygen under pressure at an elevated temperature in the presence of a metallic catalyst. The water insoluble monocarboxylic and dicarboxylic acids with from 6 to 16 carbon atoms are separated and purified by fractional distillation. The hydroxybenzyl-dialiphatic amines are combined directly with the isoparaffinic acids or in a suitable solvent. The latter is then removed by distillation.

Actions and Uses.—Unguentum Iso-Par is for external use only. It should not be covered with thick tight bandaging, since irritation may result from this type of dressing. It is said to be of value in the treatment of pruritus ani and vaginae, mycotic infections of the hand and feet and eczemas of the ear and certain skin allergic manifestations. This ointment is stimulating, lowers the levels of irritability of the skin and is in varying degrees bactericidal and fungicidal.

Dosage.—It should be applied with a rubber finger stall, a small wad of absorbent cotton or gauze, or other convenient applicator, since it possesses an odor which may be objectionable if it persists on the fingers. The first applications may cause a temporary burning sensation, but this disappears later. The ointment should be applied to the affected area in the evening before retiring and again in the morning; if necessary, it may be applied more frequently. It is claimed that the majority of cases will show evidence of response within three to five days, possibly up to two weeks. If by that time relief is not obtained, some other form of treatment should be substituted.

Tests and Standards.—

Iso-Par is a viscid, dark brown, oily liquid having a characteristic odor of burnt petroleum. It is immiscible with water; freely miscible with alcohol, volatile oil and fixed oil. The specific gravity is from 0.970 to 0.980 at 25 C.

Place about 2 cc. of iso-par in a glass stoppered cylinder, add 20 cc. of water, shake the contents for five minutes, filter through moistened paper and divide into two portions; to one portion add two drops of methyl red test solution: a distinct red color persists; to the other portion add two drops of thymol blue test solution: a distinct yellow color persists.

MEDICAL CHEMICALS

Unguentum Iso-Par: 14 Gm., 28.5 Gm., 114 Gm. and 454 Gm. jars. Contains Iso-Par 17 per cent and titanium dioxide 4 per cent in an ointment base consisting of beeswax, cetyl alcohol, lanolin and petrolatum.

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SATURDAY, OCTOBER 28, 1944

PUNISHMENT FOR VENEREAL DISEASE IN THE ARMED FORCES ENDED BY CONGRESS

The signature of the President has now enacted into law S. 1250, an act to repeal section 2 of the act approved May 17, 1926, which provides for the forfeiture of pay of persons in the military and naval service of the United States who are absent from duty on account of the direct effects of venereal disease due to misconduct, and to amend Veteran's Regulation No. 10, as amended to define line of duty and misconduct for pension and compensation purposes. S. 1250 was passed unanimously by the Senate on July 3, 1943 and by the House of Representatives on Sept. 11, 1944.

The new law abolishes all punishment for the acquisition of venereal disease, which is now "in line of duty" and is not "due to wilful misconduct," provided only that the infected person complies with Army or Navy regulations requiring him to report and receive appropriate treatment, and provided further that at the time of infection he was neither avoiding duty by desertion or absence without leave, nor confined under sentence of court martial or civil court. Failure to report a venereal infection (i. e., concealment) remains punishable by court martial or other disciplinary action at the discretion of the commanding officer (A-R 40-210, par. 23e). Moreover, the new law provides that, with the exceptions noted, veterans who have acquired venereal disease in line of duty are eligible for pension and compensation benefits if disability results.

The law is not retroactive, and a claim heretofore disallowed by reason of misconduct or line of duty requirement may not be revived; but benefits may be payable on the basis of a new claim filed hereafter in such form as may be prescribed by the Administrator of Veteran's Affairs.

The abolition of punishment for venereal disease was strongly urged by the Surgeon General, U. S. Army, by the Subcommittee on Venereal Diseases, National Research Council, and by other authorities in social hygiene and preventive medicine. Modern public health opinion is convinced that fear of punishment does not prevent exposure to venereal disease and that punitive measures promote concealment, self treatment and treatment by nonmilitary personnel. Concealment, in turn, results in continued spread of disease in the civilian population and in the armed forces themselves, and in special military hazards, as in aviators. Punishment is discriminatory, in that military personnel may be penalized not for the fact of infection but for failure to respond to treatment and for various other extraneous reasons.

Under the new law just passed, the soldier or sailor infected with a venereal disease is now on the same status as one with any other acute infectious disease. The armed forces of the United States join those of Canada and France in the abolition of punishment for illness. A public health step of the first importance has been taken.

CHRONIC GASTRITIS

In his address as retiring president of the Connecticut State Medical Society, Smith [1] discusses research on experimental gastric cancer, its background and progress. One of the stumbling blocks in the studies of human gastric cancer is chronic gastritis.

Schindler [2] holds that gastroscopy has brought convincing proof of the frequency and significance of chronic gastritis, which he divides into superficial, atrophic and hypertrophic varieties. He also reports that the histology of chronic gastritis has been established by a method of taking biopsies from the gastric wall without ligatures or clamps. "If a normal mucosa is found gastroscopically, a normal microscopic picture is usually seen also."

Schindler's remarkable work with the flexible gastroscope receives complete and enthusiastic endorsement by Crohn,[3] who characterizes "antral gasritis" as a clinical and morphologic entity, a conclusion with which Schindler does not agree. "Gastric function in all types of gastritis is so irregular and equivocal that it cannot be the basis of classification." In gastric cancer there is frequently a long story of gastric distress; Schindler refers to modern statistics as proving that patients with chronic gastritis are three times more prone to gastric carcinoma than healthy persons.

This view, as well as current interpretations of chronic gastritis, is not supported by the morphologic

1. Smith, G. M.: Comment on Experimental Gastric Cancer, Connecticut State M. J. **8**: 409 (July) 1944.
2. Schindler, R.: Gastritis in Diseases of the Digestive System (edited by Sidney A. Portis), ed. 2, Philadelphia, Lea & Febiger, 1944, p. 157.
3. Crohn, B. B.: Newer Advances in Our Knowledge of Gastritis, J. Mount Sinai Hosp. **9**: 75 (July-Aug.) 1944.

studies of the mucous membrane of the stomach at various ages by Guiss and Stewart.[4] With regard to the literature on the endoscopic aspects of chronic gastritis they say "As yet we have been unable to discover a fully correlated pathologic study made on gastroscopically diagnosed cases, nor have we had the opportunity to study enough such cases to enable us to draw any conclusions ourselves as to whether the gastroscopic diagnosis can be substantiated pathologically with uniformity."

According to Guiss and Stewart, chronic atrophic gastritis is characterized morphologically by atrophy of the mucous membrane, by increase in lymphoid tissue and in interstitial infiltration, by the transformation of the epithelial lining into the so-called intestinal or simplified type, by pyloric gland heterotopia and by increase in connective tissue. Such changes were found commonly after the fortieth year in 66 per cent of cases of death from extragastric cancer, in 82 per cent of apparently normal stomachs and in 97 per cent of deaths from gastric cancer. The inference drawn from these extensive morphologic observations is that the frequency of chronic gastritis with advancing age really may not have any other relationship to gastric cancer than intensification of gastritis by the cancer. Does early carcinoma of the stomach occur without gastritic changes?

Needed advancement in the understanding of the causation and significance of the morphologic processes of chronic gastritis will depend largely on organized cooperation by investigators concerned with the various phases of the problem. On the clinician, the gastroscopist, the radiologist and the pathologist falls the difficult task of securing adequate human material for cooperative study.

TOXICITY OF RANCID LARD

Physiologists have long recognized that rancid fats are nutritionally deleterious. According to Burr and Barnes [1] of the University of Minnesota the apparent toxic effects of rancid products are due mainly to an induced vitamin deficiency. Mixed with other foods, rancid fats destroy such essential food elements as vitamin A, carotene, vitamin D, vitamin E, pantothenic acid, pyridoxine, biotin, ascorbic acid and linoleic acid. An extreme instance of the vitamin deficiency induced by rancid fat has been reported by Fitzhugh and his associates [2] of the Food and Drug Administration, Washington, D. C.

Certain unexplainable abnormalities developed in control rats maintained for long periods on their routine laboratory diets. Fitzhugh placed 20 pairs of albino rats, 21 days of age and equally divided between the sexes, on mixed diets consisting of 18 parts of casein, 60 parts of corn starch, 5 parts of brewers' yeast, 5 parts of whole dried liver, 4 parts of salt mixture, 2 parts of cod liver oil and either 6 parts of corn oil or 6 parts of lard which had been previously stored for several months at 35 F. The two dietary mixtures were prepared in sufficient quantities to last approximately six weeks and the mixtures stored in covered tin buckets at 35 F. The rancidity of the lard was established by organoleptic tests and the peroxide number determined. This was usually 41 millimols per kilogram as contrasted with 2 millimols per kilogram in fresh lard from the same batch.

During the rapid growth period of the first three months only a slight difference was apparent in the growth rates of the rats on the corn oil and rancid fat diets. Symptoms were noted in the rancid lard group after the animals had been on this diet for about a year. Control animals on the corn oil mixture were not affected. By the end of a year the rats fed the rancid lard were emaciated, with a typical humped back and roughened coat and a rapidly progressive weakness and paralysis, usually beginning in the hind legs. The emaciation, deformity and paralysis became extreme before death.

The characteristic necropsy findings were widespread focal degenerations of the skeletal muscles. Individual muscle fibers showed varying degrees of vacuolation with gray or tan pigmentation. An occasional pigmented microphage was noted within the muscle fibers. There was also a general visceral atrophy, particularly in the uterus. This was usually small and deeply pigmented. In the male testicular atrophy occurred. Since these results are similar to the "nutritional myodegeneration" described by previous investigators [3] as characteristic of lethal vitamin E deficiency, Fitzhugh concluded that under his test conditions the main toxic effect of rancid lard was due to a complete destruction of vitamin E in his stored food mixtures. Confirming this conclusion, he found that nonrancid samples of the same batch of lard were nontoxic and nutritionally equivalent to the corn oil used in his control feedings. This is in agreement with data previously reported from the U. S. Department of Agriculture.[4]

As a practical application of these results the Washington investigators emphasize that dietary mixtures should be prepared as frequently as possible and if storage is necessary it should be at a subfreezing temperature. They found that the development of rancidity is more rapid in food mixtures than in unmixed lard and that little or no rancidity develops at 20 F.

4. Guiss, L. W., and Stewart, F. W.: Chronic Atrophic Gastritis and Cancer of the Stomach, Arch. Surg. **46**: 823 (June) 1943.

1. Burr, G. O., and Barnes, R. H.: Physiol. Rev. **23**: 256, 1943.

2. Fitzhugh, O. G.; Nelson, A. A., and Calvery, H. O.: Proc. Soc. Exper. Biol. & Med. **56**: 129 (June) 1944.

3. Mason, K. E.: Yale J. Biol. & Med. **14**: 605, 1942. Pappenheimer, A. M.: Physiol. Rev. **23**: 37, 1943.

4. Hoagland, R., and Snider, G. G.: Tech. Bull 821, U. S. Dept. Agr., 1942.

Current Comment

CHICAGO VENEREAL DISEASE CONTROL PROGRAM

A program of venereal disease control in Chicago was begun in January 1937 by the Chicago Board of Health in cooperation with the United States Public Health Service, the Federal Works Agency and the Illinois Department of Public Health. The annual report [1] for 1942-1943, has now been published. The organization of the project centers in an office of venereal control, under which are six principal subdivisions dealing respectively with clinics, the Chicago Intensive Treatment Center, education, investigation, registry and statistics, including reporting and records. The program is staffed by a venereal disease control officer, who is a surgeon in the U. S. Public Health Service, two reserve public health officers and six other division heads. The objectives of the program, as stated at its inception Jan. 2, 1937, are (*a*) to uncover all possible cases of venereal disease, (*b*) to place each newly discovered case under competent medical care, (*c*) to keep infectious cases under treatment until they are no longer a menace to society or to themselves and (*d*) to prevent new infections by all possible means, including medical, educational and legal measures. The clinic section, oldest unit of the program, is designated as the diagnostic keystone of the entire project. More than 15,000 new cases of venereal disease were diagnosed through the year. Extensive case finding and case holding methods placed and kept large numbers of spreaders of venereal disease in the Chicago Intensive Treatment Center. The educational campaign enlisted tavern owners, and those signifying their willingness to cooperate were given certificates. A Central Register was maintained of all cases of venereal disease reported to the Chicago Health Department. A register is also kept of all physicians reporting such cases. The Central Register Section received an average of 10,000 items of information per month, of which approximately 38 per cent were laboratory reports of positive serologic reactions, 27 per cent morbidity reports and 29 per cent activity reports and case dispositions, the remainder being miscellaneous items. In the Clinic Section a central clinic and eight branch clinics were operated. Over 8,600 new cases of syphilis and 8,100 cases of gonorrhea, plus 514 new cases of other venereal diseases were treated in the Clinic Section. This represented a reduction of 16 per cent in syphilis cases under treatment as compared with the end of the previous year. A social service unit operated in connection with the clinic section and was reorganized during the year to form a follow-up service. The Chicago Intensive Treatment Center, formerly the Wesley Memorial Hospital, admitted its first patients on Oct. 29, 1942. Patients stayed an average of 10.9 days in this center; 2,189 patients were admitted during the year. The report also includes extensive tabulations of venereal disease reports in the city of Chicago and an analysis of control activities.

1. Progress Report Chicago Venereal Disease Control Program 1942-1943, Board of Health, Chicago 10.

THE RELATIONSHIP OF FLUORESCENT PORPHYRINS TO CANCER

Figge and his co-workers [1] found that in a large number of vertebrates the harderian or accessory lacrimal glands excrete porphyrins, giving a red fluorescence only in the animals most susceptible to experimental cancer, namely mice, rats and hamsters. They also found that in strains of mice highly susceptible to breast cancer the harderian glands were more fluorescent than in strains of low susceptibility. These observations suggested the hypothesis that "there is a direct or indirect relationship between porphyrin metabolism and the factors that determine cancer susceptibility." Naturally, the question arose whether porphyrins accumulate in places where human cancer frequently occurs, as, for instance, in the female genital tract. Jones and his associates [2] identified porphyrins spectroscopically in red fluorescent material in various parts of the tract in about one third of the cases examined, but the occurrence of such material was not related to any definite diseases. Probably these porphyrins originate mostly from decomposition of blood. The articles cited do not claim that porphyrins are directly carcinogenic, but a good basis has been developed for further and promising studies on their relationship to carcinogenesis and other processes.

MOTIVATIONS FOR TREASON

In a lecture given before the British Psychological Society on July 1, Major A. M. Meerloo [1] of the Netherlands, a psychiatrist, whose views are presumably based on personal experience during the German occupation of his country, asks why we are so deeply affected by the idea of treachery. The traitor, he says, will not admit his treachery, but, in his own mind, his conduct is justifiable. The traitors whom he saw in his own practice were not "wicked" but were weak characters: they had been disappointed in life, they were frustrated and had transferred their feelings to political phantoms. Some were affected by serious psychiatric abnormalities; some had homosexual tendencies and had been unable to find any real basis for living. Two who took a violent part in the betrayal of Holland had a strong mother fixation, which was projected on their country. Meerloo believes these people had a grievance and desired revenge on society for real or fancied ill treatment. The desire for revenge, he points out, is the outward impulse of an inner incapacity or weakness. It is the religion of the dissatisfied and the frustrated. For the psychologist, Meerloo states, the traitor is one who needs to break away from his environment or to do violence to it and his reasons for doing so are connected with his development, particularly during adolescence.

1. Figge, F. H. J.; Strong, L. C.; Strong, L. C., Jr., and Shanbrom, A.: Fluorescent Porphyrins in Harderian Glands and Susceptibility to Spontaneous Mammary Cancer in Mice, Cancer Research **2**: 335 (May) 1942. Figge, F. H. J.: Fluorescence Studies on Cancer, ibid. **4**: 465 (Aug.) 1944.

2. Jones, E. G.; Figge, F. H. J., and Hundley, J. Mason, Jr.: The Red Fluorescence of the Genitalia of Women, Cancer Research **4**: 472 (Aug.) 1944. Figge, F. H. J.; Jones, E. G., and Wolfe, G. F.: The Extraction and Identification of Porphyrins from the Red-Fluorescent Exudates on the Genitalia of Women, ibid., p. 483.

1. Meerloo, A. M.: A Study of Treason, Lancet **2**: 321 (Sept. 2) 1944.

MEDICINE AND THE WAR

ARMY

TWENTIETH GENERAL HOSPITAL UNIT WINS HIGH PRAISE

Admiral Lord Louis Mountbatten, supreme allied commander in southeast Asia, recently presented a plaque to the 20th General Hospital, U. S. Army, in appreciation of treatment he received while suffering from an injury to his eye. Admiral Mountbatten became a patient at the army hospital after his left eyeball was cut by a branch which struck him while he was driving through the jungle on the Ledo front in Burma. During his week at the hospital in Assam Province, India, he was treated by Major Harold G. Scheie, who is credited with saving the sight of the injured eye. The plaque presented to the hospital unit has on its face a decorative design encircled by a border on which are the words "Supreme Allied Commander South East Asia." On the reverse of the plaque are the words "Presented to the 20th General Hospital, U. S. A. (Staffed by Volunteers from the University of Pennsylvania Under the Command of Colonel I. S. Ravdin), by Admiral the Lord Louis Mountbatten, G.C.V.O., C.B., D.S.O., A.D.C., Supreme Applied Commander of the Allied Forces in the South-East Asia Theatre, in Grateful Appreciation of the

Lord Mountbatten's gift: drawing of a plaque presented by the grateful British commander to the members of the 20th General Hospital, U. S. Army, who helped save his eye after a jungle accident.

Excellent Treatment He Received During the Week He Spent in the Hospital from an Injury to His Left Eye on the Ledo Front in Burma."

Appreciation of the treatment he received was also expressed by Lord Mountbatten in a letter to Colonel Ravdin, commanding officer of the hospital unit, who is on leave of absence from the Harrison professorship of surgery and the directorship of the Harrison Department of Surgical Research while serving with the army. Lord Mountbatten wrote "I am writing to thank you personally, and through you all members of the 20th U. S. General Hospital staff concerned, for the way I was looked after during my week in the hospital 7th to 14th March 1944 after receiving an injured eye. Throughout my stay I was treated with unbounded kindness and untiring attention. You can certainly be proud of the wonderful team that the University of Pennsylvania has committed to your care. If anything could increase my affection and regard for our American allies, my week with you would undoubtedly do so."

In addition, the unit has also received a captured Japanese battle flag autographed by Brig. Gen. F. D. Merrill and bears the notation "For 20th Gen. Hospital from 5307 with our thanks. Captured from Jap 18 Division near Kamaing, Burma, April 1944." In a letter to the commanding officer of the hospital unit, General Merrill paid the following tribute to the unit: "On leaving this area for another assignment I wish to express to you and all members of your staff my very sincere appreciation of the efficient medical and surgical service which you have given. I understand fully that we have added a great amount of work to an already overworked staff, but it has always been comforting to know that when my sick and wounded reached your hospital they were assured of the very best medical and surgical treatment available in this theater."

The hospital unit also received letters of commendation from Major Gen. W. E. R. Covell and Brig. Gen. Lewis A. Pick in the China-Burma-India theater.

The 20th General Hospital Unit, organized by the University of Pennsylvania, was called into active service in May 1942. It includes physicians, surgeons, dentists, nurses, technicians, Red Cross workers and enlisted personnel. The unit has been in India since early last year and is the largest American army hospital in the China-Burma-India theater.

MALARIA CONTROL IN PACIFIC PROVES SUCCESSFUL

Brig. Gen. R. W. Bliss, Assistant Surgeon General of the Army, and Brig. Gen. F. W. Rankin, director of the Surgical Consultant Division, Office of the Surgeon General, who recently returned from an inspection tour of the Pacific area, state that the malaria control activities of the Army's Medical Corps have resulted in cleaning up the South Pacific of mosquito infestation. They visited Honolulu, Maui, Canton, Mandi (Fiji Islands), Tantonto, Noumea, Espiritu Santo, Guadalcanal, Russell Island, Tarawa, Makin, Kwajalein, Saipan, Tinian and Guam. Both officers were favorably impressed with the success of the malaria control work on all these islands.

General Bliss reported on the use of a new deodorant, PDB, which has supplanted the use of crude oil to kill flies and maggots in latrines. Where 5 gallons of oil daily had been used with only limited success, half a pound of PDB powder is now sprinkled twice a week for effective deodorization. Besides the added effectiveness of the deodorant, it saves much valuable transportation, space and manpower.

AMBULANCE PRESENTED TO ARMY MEDICAL DEPARTMENT

An army ambulance was recently donated to the Medical Department of the Army by the Thomasville, N. C., Society of the National Society, Children of the American Revolution. Lieut. Col. Mason Ladd, director of the legal division of the Office of the Surgeon General, accepted the gift on behalf of the War Department.

CAPTAIN WOODROW L. PICKHARDT A PRISONER OF WAR

Capt. Woodrow L. Pickhardt, formerly of Lawton, Okla., who was reported missing in action June 7, has recently been reported to be a prisoner of war of the German government. Dr. Pickhardt is a graduate of the University of Oklahoma School of Medicine, Oklahoma City, in 1937. He entered the service Aug. 11, 1942.

TREATMENT OF GONORRHEA

In the Technical Bulletin of Medicine, No. 96, recently issued by the War Department, penicillin is stated to be the drug of choice in the treatment of gonorrhea. The use of sulfonamides will be limited to cases not responding to adequate penicillin therapy and instances in which penicillin is not available through normal supply channels.

NAME GENERAL HOSPITAL FOR DENTAL CORPS OFFICER

The War Department recently announced the naming of the Rodriguez General Hospital at San Juan, Puerto Rico, in honor of the memory of Major Fernando E. Rodriguez, U. S. Army Dental Corps. Major Rodriguez, who died in 1932, was one of dentistry's foremost research scientists, pioneering in the study of the bacteriologic aspects of dental diseases. The results of his work were so fundamental that it has been used as the basis for all further scientific research along this line. He developed new technics and methods of analysis and made many other contributions to the science of bacteriology. Major Rodriguez received a B.S. degree from Georgetown University, Washington, D. C., in 1924, after having served in the Army since 1917. He was a member of the District of Columbia Dental Society, a member of the International Association of Dental Research and a fellow of the American College of Dentists.

ARMY AWARDS AND COMMENDATIONS

Captain H. Myles Johnson

Capt. H. Myles Johnson, formerly of Fort Supply, Okla., and now attached to the famous Seagrave Hospital Unit headed by Lieut. Col. Gordon S. Seagrave, recently received a special citation from Brig. W. L. Boatner. The Seagrave Hospital Unit is with General Stilwell's forces, who are clearing northern Burma so that American engineers can extend the Ledo road to the Burma road. Dr. Johnson is credited with helping to save the lives of 2,000 Chinese soldiers on the battlefields. He has been in China, Burma, India theater of war for more than two years. Soon after the Myitkyina Airfield was captured by American and Chinese troops, the Seagrave Unit moved in. The citation reads "During this period he was under constant enemy fire, making his way over the most difficult of jungle terrain and, with utter disregard for personal safety, administered to the medical needs of both Chinese and American patients. The splendid performance of duty and disregard for personal safety reflects credit on his organization and the esprit de corps of the United States Army." Dr. Johnson graduated from the University of Oklahoma School of Medicine, Oklahoma City, in 1934 and entered the service Sept. 15, 1941.

Major George L. Thorpe

Major George L. Thorpe, formerly of Valley Center, Kan., and now a flight surgeon of a Liberator bomber group operating from an advanced air base in Italy, has been awarded the Soldier's Medal. He was decorated for the courage he displayed last February in rescuing an injured navigator from a burning plane that crashed near its home base. Unmindful of the intense heat and exploding ammunition, Dr. Thorpe rushed into the wreckage, hacking his way through burning débris to rescue a fellow officer, whom he succeeded in carrying out from what would have been a funeral pyre. Seconds later the burning ship exploded with a terrific impact, but the doctor and his charge were already safe. Dr. Thorpe graduated from Tulane University of Louisiana School of Medicine, New Orleans, in 1938 and entered the service Aug. 13, 1942.

Major Carl D. Makart

Major Carl D. Makart was recently awarded the Silver Star for gallantry in action. As soon as enemy bombs had set fire to an ammunition dump at Humboldt Bay, Dutch New Guinea, Dr. Makart, a regimental surgeon in the medical corps of the Fighting Forty-First Infantry Division, established an aid station near the scene and worked throughout the night until the following afternoon taking care of the casualties. While performing his duties Dr. Makart was in constant danger of being hit himself by shrapnel from flying bombs. Formerly of Chicago, Dr. Makart graduated from Creighton University School of Medicine, Omaha, in 1938. He was commissioned into the service Sept. 9, 1941 and was promoted to captain on Feb. 28, 1942 and to rank of major on Jan. 24, 1943.

Colonel Otis O. Benson Jr.

The Legion of Merit was awarded by the War Department to Col. Otis O. Benson Jr., formerly of Tower, Minn. The citation accompanying the award read "In his capacity as chief of Aero Medical Research at Wright Field from Sept. 6, 1940 to July 15, 1943 he was responsible for successfully developing, testing and standardizing all items of medical equipment used in connection with military aviation. His professional skill and organizing ability made it possible for his unit, during a period of rapidly changing requirements, to succeed in applying previously known principles of aviation medicine to the practical situations of modern warfare and solving new problems arising from unexpected developments in aerial combat." Dr. Benson graduated from Rush Medical College, Chicago, in 1930 and entered the service July 31, 1931.

Captain Amos V. Persing Jr.

The Bronze Star was recently awarded to Capt. Amos V. Persing Jr., formerly of Watsontown, Pa., for heroic achievement in action during the period Nov. 21, 1943 to Jan. 9, 1944 in Italy. He led his battalion medical section often under enemy artillery fire in treatment of wounded personnel. During a ten day period 500 rounds of artillery shells burst within the battalion area. This action took place at Cassino. Dr. Persing on this and other occasions in which casualties were heavy calmly and with great efficiency carried on his treatment of the wounded. Dr. Persing's action under fire reflects great credit on himself and the military service. Dr. Persing graduated from the University of Cincinnati College of Medicine in 1929 and entered the service Aug. 13 1942.

Captain Louis J. Feves

The Soldier's Medal was recently awarded to Capt. Louis J. Feves, formerly of Pendleton, Ore. The citation accompanying the award reads "for heroism displayed in the Gilbert Islands on Jan. 21, 1944. With complete disregard for his own safety he aided in the rescue of injured and recovery of deceased crew members of an airplane that had crashed on a heavily mined reef. This act of heroism reflected great credit on himself and the military service." Dr. Feves graduated from the University of Oregon Medical School, Portland, in 1935 and entered the service July 9, 1942.

Colonel Frederick J. Frese

Col. Frederick J. Frese, formerly of Yonkers, N. Y., was recently awarded the Legion of Merit for "exceptionally meritorious conduct in the performance of outstanding services in the South Pacific Area from Sept. 27, 1942 to June 1, 1944." Dr. Frese graduated from St. Louis University School of Medicine in 1938 and entered the service on completion of his internship in 1939.

Captain George H. Lage

A Presidential Citation has been issued to the parachute infantry unit to which Capt. George H. Lage, formerly of Portland, Ore., was attached as surgeon, for their work in spearheading the invasion of France and the taking of Carentan. Dr. Lage graduated from the University of Oregon Medical School, Portland, in 1939 and entered the service Sept. 22, 1942.

Captain Edward J. Doherty

Capt. Edward J. Doherty, formerly of Woodhaven, N. Y., was recently awarded the Silver Star and the Purple Heart for a leg wound which he sustained at Cherbourg. Dr. Doherty graduated from New York Medical College, Flower and Fifth Avenue Hospitals, New York, in 1934. He entered the service Aug. 7, 1942 and was sent to England in February 1944.

Colonel Walter S. Jensen

Col. Walter S. Jensen was recently awarded the Legion of Merit for "exceptionally meritorious conduct in the performance of outstanding services from July 31, 1941 until Oct. 5, 1942." Dr. Jensen graduated from the College of Medical Evangelists, Loma Linda, Calif., in 1924, and entered the service Oct. 22, 1925.

ORGANIZATION SECTION

Washington Letter

(From a Special Correspondent)

Oct. 23 1944.

Federal-State Program of Vocational Rehabilitation

Details of the expanded vocational rehabilitation program under the Federal Security Agency, recently initiated by Congress in amendments to the Vocational Rehabilitation Act (Public Law 113, 78th Congress) were outlined for THE JOURNAL today. They provide for federal aid to enable state boards of vocational education and state agencies for the blind to furnish disabled persons with all services necessary to render them employable or more advantageously employable. These services include medical and surgical care, hospitalization, physical and occupational therapy, prosthetic appliances, vocational counseling and training, maintenance during training, occupational tools and equipment, placement in employment and other necessary services.

Mentally as well as physically disabled persons are now eligible for rehabilitation. Except for certain groups of war disabled civilians and federal employees injured in line of duty, persons receiving physical restoration services or maintenance grants must be in financial need. (It was emphasized that rehabilitation of veterans with service connected disabilities is conducted through the separate program under the U. S. Veterans Administration.)

The Federal Office of Vocational Rehabilitation is responsible for establishing standards in the various areas of services, for technical assistance to the states and for certification of funds on the approval of state plans for vocational rehabilitation meeting the requirements of the authorizing act of Congress. On request, the Surgeon General of the U. S. Public Health Service has assigned Senior Surgeon (R) Dean A. Clark as chief medical officer and three other medical officers to assist in the organization of the physical restoration activities. A national professional advisory committee composed of representatives of fields of medicine actively concerned with rehabilitation, hospital administration, public health nursing, medical social work, physical therapy and occupational therapy has been appointed by the federal security administrator to assist the Office of Vocational Rehabilitation in the technical phases of physical restoration service.

State agencies have been advised of policies to be followed in organizing the physical restoration phases, and similar professional advisory committees are being appointed by all state rehabilitation agencies to guide them in establishing and maintaining professional standards for physical restoration.

Medical diagnosis and treatment of disabled persons under care of state rehabilitation agencies is limited to physicians licensed to practice medicine and surgery and otherwise qualified by training and experience to perform the specific services required. Criteria for the designation of medical specialists may include certification by the appropriate American medical specialty boards, fulfilment of the training and experience requirements for admission to examination by such boards, state agency standards for the qualification of physicians in particular specialties or approval of individual specialists by the state professional advisory committee. Rates of remuneration for physicians, nurses, dentists, physical therapists and other medical personnel for services in physical restoration are being established by state agencies in consultation with their professional advisory committees and will be similar to rates paid for similar work under state supervision, such as crippled children or workmen's compensation, or under federal supervision, such as that of the Veterans Administration or the U. S. Employees Compensation Commission. State rehabilitation agencies must purchase hospital care at inclusive rates. In approving state standards for hospital facilities the Office of Vocational Rehabilitation will for the present be guided by the list of hospitals approved by the American College of Surgeons. Preference will be given to hospitals having more than 100 beds with well developed specialty services, medical social service, physical therapy and occupational therapy, in view of special requirements. Eligible to receive the service are any person in the United States, District of Columbia, Puerto Rico and Hawaii who has a disability that is (1) a substantial employment handicap, (2) static or (3) remediable to a substantial extent in a reasonable time. Said a spokeman "Vocational rehabilitation is designed to conserve the working usefulness of the civilian disabled. In restoring a disabled person to productive work he is being transferred from the public assistance rolls to the payrolls of industry, by which he resumes his status as a self-supporting member of the community."

Medical Economic Abstracts

Progress of Medical Service Plans

To form a basis for mutual comparison, the various medical society prepayment plans were asked by the Bureau of Medical Economics for as recent a financial report as it was possible to give. Some of the principal items of the reports received are given here. Copies of these reports in full are available for administrators of all existing and proposed plans.

Surgical Care, Inc.—This was organized late in 1942 to serve Jackson County, Mo., and Wyandotte County, Kan. Its contracts covered surgery, obstetrics, anesthesia and x-ray. On Jan. 31, 1944 it had a membership of 3,525 males and 5,144 females, including subscribers and dependents. Its income from subscribers up to Jan. 31, 1944 was $23,448, of which it expended $18,323.96 and now has a surplus of $5,124.04.

Medical Expense Fund of New York, Inc.—According to recent advices (THE JOURNAL, May 27, p. 296) the Medical Society of the State of New York has unanimously endorsed the merger of the Community Medical Care, Inc., a medical insurance affiliate of the Associated Hospital Service, which has 43,000 subscribers, and the Medical Expense Fund of New York, Inc., with 1,200 subscribers. The new group will be known as United Medical Services.

Medical Service Association of Pennsylvania.—This was organized in June 1940 and serves the state of Pennsylvania. It offers only surgical contracts, and as of Dec. 31, 1943 it had 3,086 subscribers and 5,631 dependents, making a total of 8,717 entitled to service. Its income to the date given was $45,722.02 and expenditures $45,796.57, showing a loss of $74.55 on operation. It had on hand a reserve of $25,631.72.

Society Proceedings

COMING MEETINGS

American Academy of Pediatrics, St. Louis, Nov. 9-11. Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill., Secretary.

American Society for the Hard of Hearing, New York, Nov. 10-12. Mr. Raymond H. Greenman, 1537 Thirty-Fifth St., N.W., Washington 7, D. C., Managing Director.

Annual Conference of State Secretaries and Editors, Chicago, Nov. 17-18. Dr. Olin West, 535 N. Dearborn St., Chicago, Secretary.

Association of Military Surgeons of the United States, New York, Nov. 2-4, Col. James M. Phalen, Army Medical Museum, Washington 25, D. C., Secretary.

Central Neuropsychiatric Association, Chicago, October 31. Dr. Ernest M. Hammes, 1124 Lowry Medical Arts Bldg., St. Paul 2, Minn., President.

Central Society for Clinical Research, Chicago, Nov. 3-4. Dr. Carl V. Moore, 602 S. Euclid Ave., St. Louis 10, Secretary.

Midwestern Section of American Federation for Clinical Research, Chicago, Nov. 2. Dr. Richard H. Lyons, University Hospital, Ann Arbor, Mich., Secretary.

New York State Association of Public Health Laboratories, Albany, Nov. 17. Miss Mary B. Kirkbride, New Scotland Ave., Albany 1, Secretary.

Puerto Rico, Medical Association of, Santurce, Dec. 15-17. Dr. E. Martinez-Rivera, P. O. Box 3866, Santurce, Secretary.

Southern Medical Association, St. Louis, Mo., Nov. 13-16. Mr. C. P. Loranz, Empire Building, Birmingham 3, Ala., Secretary.

Western Surgical Association, Chicago, Dec. 1-2. Dr. Arthur R. Metz, 250 East Superior St., Chicago, Secretary.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CONNECTICUT

Society Programs.—"The Future of Prepayment Medical Plans" was discussed before the Fairfield County Medical Association in Stamford, October 4, by Dr. Louis H. Bauer, Hempstead, N. Y. Other county medical programs in the state during October included:

Hartford County Medical Association, October 24, Hartford, symposium on the treatment of burns from the circus fire.
Litchfield County Medical Association, October 3, Washington, Lieut. Comdr. William E. Neff Jr. (MC), "Medical Experiences in Guadalcanal," and Major Charles C. Verstandig, M. C., "The Landing at Casablanca."
Middlesex County Medical Association, October 12, Cromwell, Dr. John R. Paul, New Haven, "Virus Diseases in the Present War."
New Haven County Medical Association, October 26, Waterbury, Dr. Percy S. Pelouze, Philadelphia, "Gonorrhea and Its Treatment," and Karl F. Heizer, Ph.D., "Chronic Illness in Connecticut."
New London County Medical Association, October 5, Norwich, Dr. Meredith F. Campbell, New York, "Common Urinary Tract Infections in Children."
Tolland County Medical Association, October 17, Somers, Dr. Francis G. Blake, New Haven, "The Treatment of Infections with Penicillin."
Windham County Medical Association, October 19, Putnam, Dr. William T. Salter, New Haven, "Recent Advances in Therapy."

ILLINOIS

Meeting of Bacteriologists.—The fall meeting of the Society of Illinois Bacteriologists will be held at Huyler's Restaurant, Chicago, November 3. The speakers will be:

Stewart A. Koser, Ph.D., and Grace R. Baird, M.A., Chicago, Bacterial Destruction of Nicotinic Acid.
Joseph Zichis, Ph.D., Chicago, Viruses Causing Pneumonia and Laboratory Methods of Recognizing Them.
Robert R. Fulton, Ph.D., Chicago, Thermophilic Bacteria and Aerobic Decomposition of Soluble Carbohydrates in Distillery Effluent.

District Meeting.—The Illinois State Medical Society sponsored a postgraduate conference for central Illinois in cooperation with the seventh district at the Hotel Orlando, Decatur, October 26. In addition to a series of round table discussions the following spoke:

Dr. Oswald P. J. Falk, St. Louis, Recognition and Management of Coronary Disease.
Dr. Frederick W. Slobe, Chicago, Industrial Surgery.
Dr. Clarence A. Neymann, Chicago, The Present Day Treatment of Syphilis of the Central Nervous System.
Major Paul L. Shallenberger, M. C., Amebiasis.
Lieut. Col. Willoughby P. Richardson, M. C., Neuropsychiatric Problems and the War.

Chicago

The D. J. Davis Lectureship.—Henry B. Ward, Ph.D., professor of zoology emeritus, University of Illinois, will deliver the annual D. J. Davis Lecture at the University of Illinois College of Medicine, November 13, at 1 o'clock in the afternoon. His subject will be "Medical Zoology in America's First Century." The lecture was established in 1943 by the associates and friends of Dr. Davis on his retirement as dean at the medical school.

Dr. Strecker to Give Pasteur Lecture.—Dr. Edward A. Strecker, professor of psychiatry, University of Pennsylvania School of Medicine, Philadelphia, will deliver the seventeenth annual Pasteur Lecture of the Institute of Medicine of Chicago, November 2, at the concluding session of the Institute of Medicine's Postgraduate Assembly on Nervous and Mental Diseases at the Palmer House (THE JOURNAL, September 9, p. 114). Dr. Strecker's subject will be "War Psychiatry and Its Influence on Postwar Psychiatry and Civilization."

Medical Talks.—On October 22, Dr. Louis R. Limarzi discussed "Blood—The Human Life Line," the first in a series of lectures now being given at the Museum of Science and Industry on Sunday afternoons. Others in the series will include:

Dr. Robert S. Berghoff, Your Heart, What You Should Know About It, October 29.
Dr. Clifford J. Barborka, Your Diet in Health and Disease, November 5.
Dr. Carroll C. L. Birch, Bugs Are Worse Than Bullets, November 12.
Dr. W. W. Bauer, Director, Bureau of Health Education, American Medical Association, Stop Annoying Your Children, November 19.
Dr. Leo K. Campbell, Too Fat, Too Thin, November 26.

Committee on Allocation of Dogs from City Pound.—A committee has been appointed to advise Dr. Herman N. Bundesen, president of the Chicago Board of Health, in the allocation of dogs from the city pound for medical experimentation purposes. Members of the committee include Dr. Ole C. Nelson, medical director of the Cook County Hospital; Rev. Preston Bradley, pastor of the Peoples Church; Mrs. Charles Petkus, vice president of the Illinois Citizens Animal Welfare League; Wesley A. Young, D.V.M., managing director of the Anti-Cruelty Society, and:

R. Wendell Harrison, Ph.D., associate dean of biologic sciences at the University of Chicago.
John J. Sheinin, Ph.D., dean of the Chicago Medical School.
Seaver A. Tarulis, D.O., head of the Chicago College of Osteopathy.
Dr. Raymond B. Allen, dean of the University of Illinois College of Medicine.
Dr. Italo F. Volini, dean of Loyola University School of Medicine.
Dr. George H. Gardner, assistant dean of Northwestern University Medical School.

INDIANA

State Medical Election.—Dr. Jesse E. Ferrell, Fortville, was named president-elect of the Indiana State Medical Association at its annual meeting in Indianapolis, October 5, and Dr. Nelson K. Forster, Hammond, was inducted into the presidency. Dr. Arthur F. Weyerbacher, Indianapolis, was reelected treasurer and Mr. Thomas A. Hendricks, Indianapolis, executive secretary for his twentieth term. French Lick was selected as the site for the 1945 convention.

KENTUCKY

Cancer Control Program.—The Kentucky General Assembly at its 1944 session appropriated $15,000 for each of the next two years with the stipulation that these funds be made available to the state department of health for use in connection with the program of the Field Army and the Kentucky division of the American Cancer Society. A number of meetings have been held between Dr. Francis Guy Aud, Louisville, chairman, executive committee of the Kentucky division, Dr. Philip E. Blackerby, Louisville, state health commissioner and the general chairman of the Kentucky Field Army, to consider distribution of the funds. Prior to the appropriation, diagnostic cancer clinics were established in Louisville, Lexington and Middlesboro. The Campbell-Kenton County Medical Society has authorized the establishment of a diagnostic cancer clinic at the William Booth Memorial Hospital, Covington, in collaboration with other hospitals, and consideration is now being given by local societies for the establishment of similar diagnostic clinics at Paducah, Owensboro and Ashland, according to the *Kentucky Medical Journal*. Applications for admission to the clinics will be made through the local boards of health. The funds appropriated by the assembly will be made available for the payment of hospital services of patients who remain in affiliated hospitals for treatment, it was stated.

MICHIGAN

State Medical Election.—Dr. Vernor M. Moore, Grand Rapids, was chosen president-elect of the Michigan State Medical Society at its annual meeting in Grand Rapids in September, and Dr. Andrew S. Brunk, Detroit, was inducted into the presidency. The 1945 session will be held in Detroit, September 19-21.

Bequest for Graduate Medical Education.—The late Dr. Andrew P. Biddle, Detroit, formerly president of the Michigan State Medical Society, who died August 2, bequeathed about $40,000 to the society's Foundation for Post-Graduate Medical Education. The late physician has been a leader in the postgraduate medical program directed by the state medical society, which, for a number of years, has been presenting an annual oration bearing his name.

Public Health Conference.—The twenty-fourth annual meeting and the third wartime Michigan Public Health Conference will be held at the Hotel Pantlind, Grand Rapids, November 8-10. Among the speakers will be John M. Hepler, C.E., Lansing, president of the Michigan Public Health Association, Dr. William DeKleine, state health officer, Lansing, and Henry F. Vaughan, Dr.P.H., Ann Arbor, dean, School of Public Health, University of Michigan. One of the features of the meeting will be a progress report of the mosquito survey now being conducted by the state department of health.

Hospital Prizes.—At a staff meeting of Mount Carmel Mercy Hospital, Detroit, September 20, four interns and residents received prizes for papers presented for their graduation. Dr. Joseph W. Geppert and J. Earle Estes received first and second prize for interns, respectively, for their work on "Acute Pancreatic Necrosis" and "A Case of Spontaneous Hypoglycemia." For the residents, first and second prizes, respectively, went to Drs. Leonard J. Janis and John Dedinsky for their work on "A Handful of Valuable Suggestions

(greeting the oncoming extern and intern)" and "Science vs. Art of Medicine in the Treatment of Fracture of the Patella." First prize in both groups was $100 and second $50.

Faculty Changes.—Dr. Henry Field Jr. has resigned as professor of internal medicine, University of Michigan Medical School, Ann Arbor, to enter private practice in Buffalo and to serve as associate professor of internal medicine at the University of Buffalo School of Medicine. Dr. Field, who graduated at Harvard Medical School, Boston, in 1920, had been a member of the Michigan faculty since 1926, when he had been named assistant professor of internal medicine. He had been professor since 1941. Dr. Carl A. Moyer, assistant professor of surgery at Michigan, resigned effective September 1 to accept a position as director of surgery at the William J. Seymour Hospital, Eloise. Before obtaining his degree of medicine at Michigan in 1937 Dr. Moyer had served in the departments of physiology, anatomy and pharmacology. In 1943 he received the Henry Russel Award, which is presented annually to a member of the university for outstanding work (THE JOURNAL, June 12, 1943, p. 454).

NEW YORK

Competition for Prize Essays.—The Merrit H. Cash Prize and the Lucien Howe Prize are open for competition for presentation at the 1945 meeting of the Medical Society of the State of New York. The Lucien Howe Prize of $100 will be presented for an original contribution on some branch of surgery, preferably ophthalmology. The author need not be a member of the Medical Society of the State of New York. The Merrit H. Cash Prize of $100 will be given to the author of the best original essay on some medical or surgical subject. Competition is limited to the members of the Medical Society of the State of New York who at the time of the competition are residents of New York State. All essays must be presented not later than Feb. 1, 1945 and sent to Dr. Charles Gordon Heyd, chairman of the committee on prize essays of the state medical society, 292 Madison Avenue, New York 17.

New York City

Oswald Avery Honored.—Dr. Oswald T. Avery, for thirty years a member of the staff of the Rockefeller Institute for Medical Research and since 1943 emeritus member, received the gold medal of the New York Academy of Medicine for distinguished service in medicine at a meeting October 5. Presentation was made by Dr. Arthur Freeborn Chace, president of the academy, and the citation acknowledged that Dr. Avery's "investigations have led to discoveries and great advances in the science of bacteriology."

Compensation Committee Created.—The formation of a medical practice committee by Edward Corsi, state industrial commissioner, was announced October 6. The new unit will have jurisdiction over all physicians and surgeons practicing in workmen's compensation cases in New York City with the exception of Richmond County. Dr. Francis M. Conway, New York, was named chairman and Drs. Edwin Welles Kellogg, New York, and Joseph Raphael, Brooklyn, were named associates. The creation of the committee was authorized by an act of the 1944 legislature that gave control over compensation practice to the state industrial commissioner, according to the New York *Times*. Heretofore all controls over physicians practicing in these cases were under the supervision of county medical societies. The new law, however, was said to be the outgrowth of the exposure of the "kickback racket."

First Human Rabies Death in Eight Years.—The occurrence of a case of human rabies in the Bronx, the first recorded in the borough for more than eight years, was disclosed October 9. The victim, a woman aged 53, contracted the disease as a result of being bitten by her own dog August 25; she died September 13. Official announcement of the death was withheld by the city health department until the completion of special laboratory tests confirming the diagnosis of rabies. The woman and her daughter were both bitten on the hand while handling the dog August 25. The same day, while the animal was being taken to an animal shelter, the dog caused a severe laceration on the woman's lip. She was immediately given antirabic treatment, and a series of injections had not been completed when she first became ill. She was hospitalized September 10 and became rapidly worse until she died September 13. On October 16 the antirabies quarantine which has been in effect in the Bronx since March 30 was ordered by Health Commissioner Ernest L. Stebbins extended throughout the city.

The Salmon Lectures.—Brigadier John R. Rees, consulting psychiatrist to the British army and medical director, the Tavistock Clinic (the Institute of Medical Psychology), will deliver the Salmon Lectures for 1944 at the New York Academy of Medicine, November 20-22. The title of his lectures will be "The Frontiers Extend," "Opportunities Emerge" and "The Way Ahead." Following the lectures at the academy Dr. Rees will tour the country in the following itinerary:

Date	Place	Co-Sponsors
November 25	New Orleans	New Orleans Society of Neurology and Psychiatry.
November 26	San Antonio	Hogg Foundation for Mental Hygiene
November 27	Houston	and various medical groups.
November 30	Los Angeles	Los Angeles Academy of Medicine.
December 1	Boston	Massachusetts Psychiatric Society.
December 7	Montreal	Medical Chirurgical Society of Montreal.

The Salmon Committee on Psychiatry and Mental Hygiene, appointed by the council of the New York Academy of Medicine, annually invites a prominent specialist in the field of psychiatry, neurology or applied sciences, who has made the greatest contribution to his specialty during the preceding year, to deliver the lecture series.

MONTANA

Plague Infection.—Plague infection has been proved in a pool of 50 fleas from 20 prairie dogs, Cynomys ludovicianus, collected on July 26 on a ranch 20 miles northeast of Hardin, according to *Public Health Reports.*

OHIO

Physician Wills Fund to Academy.—The Academy of Medicine of Cincinnati has received more than $7,000 under the will of the late Dr. Meyer K. Amdur, who became a member of the academy Nov. 17, 1942 and who died July 15, 1943. It is reported that two other items in the will may eventually yield several hundred dollars more for the academy's benefit.

University Postgraduate Day.—The eleventh annual postgraduate day of the Medical Institute of the University of Toledo will be held November 3 at Toledo. Among the speakers will be:

Col. Joseph C. Bell, M. C., Roentgenographic Chest Studies as Seen in the Percy Jones Hospital and Rupture of the Intervertebral Disk, with Extrusion of a Portion of the Disk into the Spinal Canal, as a Cause of Low Back and Lower Extremity Pain.
Col. Byrl R. Kirklin, M. C., Place of the Cholecystogram in the Diagnosis of Gallbladder Disease and Gastrointestinal Conditions Revealed by X-Ray.
Dr. Ursus V. Portmann, Cleveland, Irradiation in Cancer of the Breast.
Dr. Lawrence Reynolds, Detroit, Pseudo Fractures and Some Medicolegal Problems in Connection with General Practice.

A feature of the meeting will be a memorial session in honor of the late Dr. John T. Murphy.

PENNSYLVANIA

Hospital News.—Under a building program for which contracts were let September 27, a new power plant and alterations to the main hospital building of the George F. Geisinger Memorial Hospital, Danville, will be constructed. The alterations will include expansions to the obstetric department and increase the bed capacity for mothers from 20 to 37 and the infant bassinet capacity from 20 to 35. The fourth floor of the main hospital building will be devoted entirely to a suite of two delivery rooms and four labor rooms, quarters for the preparation of sterile supplies and sleeping quarters for staff physicians on obstetric service. The estimated cost will be about $300,000.

Philadelphia

Portrait of Dr. Hatfield.—An oil portrait of Dr. Charles J. Hatfield, president of the Philadelphia Tuberculosis and Health Association, has been hung in the Henry Phipps Institute, the gift of friends throughout the country to honor him for his forty years service in the field of tuberculosis. Dr. Hatfield is secretary of the National Tuberculosis Association and one of its founders.

Personal.—Theodore Anton Phillips, director of medical department sales of the J. B. Lippincott Company, has been appointed director of medical and scientific publications of the Blakiston Company.——Dr. Edward B. Krumbhaar, professor of pathology in the University of Pennsylvania School of Medicine and Graduate School, has been elected an honorary fellow of the Royal Society of Medicine, London, "in recognition of his distinguished services to science."

Pittsburgh

Special Society Elections.—Dr. John D. Sturgeon Jr., Uniontown, is president of the Pittsburgh Pediatric Society, Dr. Joseph S. Baird vice president and Dr. Christian J. Stoecklein secretary-treasurer.——Dr. Kenneth E. Appel, Philadelphia, was chosen president-elect of the Pennsylvania Psychiatric Society at its sixth annual dinner meeting at the University Club, September 21, and Dr. George W. Smeltz was installed as president. Dr. LeRoy M. A. Maeder, Philadelphia, is secretary and Dr. Ralph L. Hill, Wernersville, the immediate past president. Speakers at the meeting included Comdr. James M. Henninger (MC) on "Navy Psychiatry, with Particular Reference to the South Pacific" and Lieut. Col. Baldwin L. Keyes, M. C., "Psychiatry in the Middle East."

TENNESSEE

Dr. Diggs Goes to Cleveland Clinic.—Dr. Lemuel W. Diggs, since 1938 associate professor of medicine at the University of Tennessee College of Medicine, Memphis, has accepted an appointment as clinical pathologist in charge of the clinical laboratories of the Cleveland Clinic, Cleveland, effective January 1. Dr. Diggs graduated at Johns Hopkins University School of Medicine, Baltimore, in 1926 and was for three years a member of the department of medicine at the University of Rochester School of Medicine and Dentistry, Rochester, N. Y. He has been directing his attention to sickle cell anemia.

GENERAL

Anesthesia Session Planned.—Investigators wishing to present material for clinical research before the Eastern section of the American Federation for Clinical Research at a meeting in Boston, December 9, are urged to communicate with Dr. Orville T. Bailey, Harvard Medical School, 25 Shattuck Street, Boston, before November 15. An abstract of not over two hundred words should be submitted.

Louis Dublin Serves as Temporary Head of Red Cross.—Louis I. Dublin, Ph.D., New York, second vice president and statistician of the Metropolitan Life Insurance Company, on October 2 became temporary executive officer of the American Red Cross and will serve in this capacity until the return of Basil O'Connor, who is now on an inspection tour of Red Cross operations in France and Great Britain. Dr. Dublin is on loan to the Red Cross for a limited period. His normal assignment is as assistant to Mr. O'Connor, acting as coordinator of the various operating divisions of the Red Cross. In his new appointment Dr. Dublin will devote full time to Red Cross activities.

Annual Forum on Allergy.—The seventh annual Forum on Allergy will be held in the Hotel William Penn, Pittsburgh, January 20-21. A feature of the meeting will be the first award of the Marcelle Prize, established by the Marcelle Cosmetics, Inc., Chicago, in 1944 to be awarded to the author of the best paper on allergy appearing in the American medical literature during the year. The first prize will be for $350 and the second for $150. Physicians attending the session will have access to twelve study groups in addition to special lectures, motion pictures, demonstrations, symposiums and panel discussions. On Friday evening preceding the forum the American Association of Allergists for Mycological Investigation will hold its annual meeting, at which time the results of its cooperative research on allergy to fungi will be reviewed.

Meeting of Anesthetists.—The American Society of Anesthetists will meet in the Rice Hotel, Houston, November 2, and at the University of Texas Medical Branch, Galveston, November 3, as guests of the Texas Association of Medical Anesthetists. In addition to clinical demonstrations and round table discussions the following will speak:

Dr. Robert L. Sanders, Memphis, Tenn., Surgeon-Anesthetist Relationship.
Dr. Hubert R. Hathaway, San Francisco, The Postoperative Ambulatory Patient.
Lieut. Col. William J. Winter, M. C., and Comdr. Jarvis C. Youngblood (MC), War Anesthesia.
Dr. Ralph M. Waters, Madison, Wis., Imperfections of Inhalation Anesthesia.

At the dinner meeting Thursday evening speakers will include Dr. Ernst W. Bertner, Houston, on "Anesthesia in the Development of Surgery" and Chauncey D. Leake, Ph.D., Galveston, "The Centennial of Anesthesia."

Award in Mental Hygiene Created.—The Albert and Mary Lasker Foundation, Inc., has established the Lasker Award of $1,000 to be given annually through the National Committee for Mental Hygiene for outstanding service in the field of mental hygiene. The new award will be conferred at the annual meeting of the committee in the autumn of each year. The purpose of the award is to recognize significant contributions to promoting mental hygiene and to making the broad field and program of mental hygiene more familiar to the general public. Each year the award will be made for a contribution in some special aspect of the field of mental hygiene which seems to be of most immediate and current significance. The recipient of the award will be selected by an anonymous jury chosen annually for its competence to judge accomplishment in a particular field. The award this year will be for mental hygiene work related to the war. The recipient will be chosen from among leaders who have done work in the general enhancement of the mental health of the men and women of the services, both while in service and during the period of rehabilitation, so far as developed at the time. The work must either have been completed or have been tested and won general acceptance within the year preceding the granting of the award. Recipients will not necessarily be limited to persons in the United States. If some outstanding contribution has been made abroad in a particular field, the award will be made jointly with the leading mental hygiene organization of that foreign country.

Industrial Hygiene Foundation.—The ninth annual meeting of the Industrial Hygiene Foundation of America will be held at the Mellon Institute, Pittsburgh, November 15-16. The theme of the meeting will be "Postwar Industrial Health." Among the speakers will be:

Dr. Hallowell Davis, Boston, Protection of Workers Against Noise.
Dr. Leonard E. Himler, Ann Arbor, Mich., Practical Psychiatry in Industry.
George R. Hill, Ph.D., Salt Lake City, Effectiveness of Tall Stacks in Minimizing Air Pollution from Industrial Plants.
Lieut. Col. Theodore F. Hatch, S. C., Upper Limits of Tolerance to Heat and Humidity.
Francis R. Holden, Ph.D., and W. C. L. Hemeon, M. S., Pittsburgh, Findings from Foundation Surveys of War Plants.
Dr. George W. Wright, Saranac Lake, N. Y., Medical Aspects of Compensation for Partial Disability from Silicosis.
Theodore C. Waters, Baltimore, Legal Aspects of Compensation for Partial Disability from Silicosis.
Marshall Dawson, Washington, D. C., Second Injury Funds as Employment Aids to the Handicapped.
Vandiver Brown, New York, Legal Developments in 1944 Respecting Industrial Health.
Andrew Court, Detroit, The Economic Basis of Health.
William M. Gafafer, D.Sc., Washington, D. C., Sickness Indemnification.
Nathan Sinai, D.P.H., Ann Arbor, Mich., Medical Expense Indemnification.
Dr. Carl M. Peterson, Secretary, Council on Industrial Health, American Medical Association, Chicago, Recent Developments in Preplacement Physical Examinations.
V. P. Ahearn, executive secretary, National Industrial Sand Association, Increasing Importance of Industrial Health in Industrial Relations.

One session on "Putting the Disabled Veteran Back to Work" will be presided over by Dr. Clarence D. Selby, medical consultant, General Motors Corporation, Detroit.

Academy of Pediatrics.—The American Academy of Pediatrics has designated its meeting at the Hotel Jefferson, St. Louis, November 9-11, as a "Wartime Conference on Child Health." One session will be devoted to the control of rheumatic fever with the following speakers: Drs. Alexander T. Martin, New York; Rene Wegria, New York; Alexis F. Hartmann, St. Louis; Ann G. Kuttner, Irvington, N. Y.; T. Duckett Jones and Benedict F. Massell, Boston; Col. Leonard G. Rowntree, M. C.; John George Fred Hiss, Syracuse; George M. Wheatley, New York; Betty Huse, Washington, D. C.; Paul F. Dwan, Minneapolis; Louise F. Galvin, Richmond, Va., and Clark H. Hall, Oklahoma City. Other speakers on the program will include:

Dr. Madge T. Macklin, London, Ont., Erythroblastosis Fetalis.
Dr. Gerardo Varela, Jacuba, Mexico, Bacterial Dysenteries.
Drs. Grover F. Powers and Paul L. Boisvert, New Haven, Conn., Age as a Factor in Streptococcoses.
Dr. Wallace E. Herrell, Rochester, Minn., Penicillin, Its Use in Pediatrics.
Dr. Leslie Nelles Silverthorne, Toronto, Whooping Cough.
Dr. Hattie E. Alexander, New York, Treatment of H. Influenzae Infections in Children.
Dr. John A. Toomey, Cleveland, The Neuropathies.
Ernest Carroll Faust, Ph.D., New Orleans, Arthropod Borne Diseases.

A special feature of the meeting will be a symposium on parenteral therapy conducted by Dr. Hartmann and Drs. Allen M. Butler, Boston; Luther Emmett Holt Jr., Baltimore, and Sam Z. Levine, New York.

College of Surgeons Expands Graduate Training Program.—The American College of Surgeons announces the appointment of Major Gen. Charles R. Reynolds, M. C., retired, former surgeon general of the U. S. Army, as consultant in graduate training in surgery and of Dr. George H. Miller, dean and professor and head of the department of medicine, American University of Beirut, Beirut, Lebanon, as

director of educational activities. The appointments are part of an expanded program of graduate training in surgery of the college. Both physicians will have offices at the Chicago headquarters of the college. The department of graduate training in surgery is under the direction of Dr. Malcolm T. MacEachern, Chicago, chairman of the administrative board of the college. It will be responsible to the committee on graduate training in surgery and to the board of regents. In addition to General Reynolds and Dr. Miller, the staff of the department will consist of Dr. Paul S. Ferguson, director of surveys, three assistants who conduct the surveys, and the field representatives conducting the regular hospital standardization surveys under the direction of Dr. Earl W. Williamson, assistant director of the college, who aid as required in the graduate training program. The latter is a development of the basic work of the college in stimulating the improvement of hospital service. General Reynolds is leaving his position as director of the Pennsylvania state bureau of tuberculosis control, Harrisburg, Pa., where he has been serving for the past four years, to accept the new appointment. He was commandant of the Army Field Service Medical School, Carlisle Barracks, Pa., from September 1923 to 1931 and surgeon general of the Army for a four year term beginning 1935.

Western Surgical Association.—The fifty-second annual meeting of the Western Surgical Association will be held at the Drake Hotel, Chicago, December 1-2. At the annual dinner Friday evening the president of the association, Dr. Willis D. Gatch, Indianapolis, will speak on the "Prospects of Our Association." Other speakers will be Dr. Herman L. Kretschmer, President, American Medical Association, Chicago, and Capt. E. Eric Larson (MC) on "The Medical Aspects of Our War in the Pacific." Among other speakers on the program will be:

Dr. Francis E. Clough, San Bernardino, Calif., Madura Foot.
Dr. Neil J. MacLean, Winnipeg, Man., The Technic for Closure of the Ring of Postoperative Abdominal Hernia.
Dr. Jacob K. Berman, Indianapolis, Interscapulothoracic Disarticulation of the Arm.
Drs. Erwin R. Schmidt, Ralph M. Waters and Noel A. Gillespie, Madison, Wis., Postoperative Deaths.
Dr. Arnold S. Jackson, Madison, Use of Thiouracil in the Treatment of Hyperthyroidism.
Dr. Martin C. Lindem, Salt Lake City, Thyroidectomy by the Off the Trachea Method.
Dr. Herbert H. Davis, Omaha, Amino Acids Used Intravenously in Surgical Patients.
Drs. Earl C. Padgett, Kansas City, Mo., and John H. Gaskins, Use of Skin Flaps in the Repair of Scarred or Ulcerative Defects over Bone and Tendons.
Dr. Louis P. Good, Texarkana, Texas, Origin and Growth of an Adenoma of the Islands of Langerhans.
Drs. Stanley R. Maxeiner and Col. Harry E. Bundy, M. C., Resection of Pancreas for Hyperinsulinism.
Drs. Warren H. Cole and John T. Reynolds, Chicago, Resection of the Duodenum and Head of the Pancreas for Carcinoma.
Dr. Thomas G. Orr, Kansas City, Pancreaticoduodenectomy for Carcinoma of the Ampulla.
Dr. J. Dewey Bisgard, Omaha, Gastric Resection for Certain Acute Perforated Lesions of the Stomach and Duodenum with Diffuse Soiling of the Peritoneal Cavity.
Dr. Stuart W. Harrington, Rochester, Minn., Surgical Treatment of Pharyngo (Esophageal) Diverticulum (Review of 140 Cases).
Dr. Robert L. Sanders, Memphis, Tenn., Review of One Hundred Subtotal Gastrectomies for Benign Ulcer.
Dr. Henry K. Ransom, Ann Arbor, Mich., Gastrojejunocolic Fistula.
Drs. Claude F. Dixon and Raymond E. Benson, Rochester, Surgical Management of Sigmoidal Carcinoma Involving the Urinary Bladder.
Dr. Owen H. Wangensteen, Minneapolis, Preservation of the Sphincters and Intestinal Continuity in Operation for Carcinoma of the Rectal Ampulla.
Drs. Charles G. Johnston and Elisha S. Gurdjian, Detroit, Peripheral Nerve Injury in Association with Fractures of Long Bones.
Drs. Loyal Davis, George E. Perret and Walter W. Carroll, Chicago, Repair of Peripheral Nerves in the Presence of Extensive Soft Tissue and Bone Injuries of the Extremities.
Dr. Henry W. Meyerding, Rochester, Chronic Sclerosing Osteitis: Differential Diagnosis.
Dr. Kellogg Speed, Chicago, Treatment of Infected Pin Operations for Fractures of the Neck of the Femur.
Dr. Melvin S. Henderson, Rochester, Status of the Bone Graft in Ununited Fractures of the Neck of the Femur.
Dr. Glen Evan Cheley, Denver, Personal Evaluation of Vitallium Cup Arthroplasty of the Hip Joint.

Southern Medical Association.—The thirty-eighth annual meeting of the Southern Medical Association will be held at the Municipal Auditorium and the Jefferson Hotel, St. Louis, November 13-16, under the presidency of Dr. James A. Ryan, Covington, Ky., who assumed the position on the death, May 2, of Dr. William T. Wootton, Hot Springs National Park, Ark. The first general public session has been designated President's Night, at which Dr. Ryan will discuss "The Public's Obligation to the Medical Profession." Other speakers will include Dr. Herman L. Kretschmer, President, American Medical Association, Chicago, on "The Progress of Medicine During the Past Fifty Years," and Major Albert J. Stowe, G. S. C., "Be Vigilant and Mum!" A feature of this meeting will be the presentation of the Leslie Dana Gold Medal by the St. Louis Society for the Blind to Miss Linda Neville, Lexington, Ky. (THE JOURNAL, July 8, p. 730). A second public session Wednesday evening will be devoted to "Medicine in the War," at which the speakers will be Capt. Alphonse McMahon (MC), on "Civilian Tropical Disease Problems Following Demobilization"; Col. Howard A. Rusk, M. C., "New Horizons in Medicine," and Rear Admiral Luther Sheldon Jr. (MC), "Navy Medicine in the War." Among the many speakers on the program, which is further divided into general clinical and sectional sessions, are:

Dr. William C. MacDonald, St. Louis, Thiouracil in the Management of Hyperthyroidism.
Drs. Vincent de P. J. Derbes, Hugo T. Engelhardt and Theodore A. Watters, New Orleans, Management of Migraines.
Dr. George T. Harrell Jr., Dr. William L. Venning Jr. and William A. Wolff, Ph.D., Winston-Salem, N. C., Treatment of Rocky Mountain Spotted Fever.
Dr. John T. Howard, Baltimore, Experiences with the Gastroscope over a Period of Six Years.
Dr. Charles F. Mohr, Baltimore, Results of Penicillin Treatment in Neurosyphilis.
Capt. Arthur C. Allen, M. C., and Dr. Sophie Spitz, M. C., Pathology of Scrub Typhus (Tsutsugamushi Fever).
Drs. Walter S. Lawrence and Walter W. Robinson, Memphis, Radiosensitive Parasellar Tumors: Case Reports.
Dr. Harry S. Bernton, Washington, D. C., Castor Bean Sensitiveness: Case Report.
Capt. Frederick A. Jostes (MC), Physical Medicine: Its Importance in Any Rehabilitation Program.
Col. John C. Burch, M. C., and Lieut. Col. Herbert C. Fisher, M. C., Appendicitis Mortality.
Dr. Robert A. Knight, Memphis, Treatment of Fractures of the Tibial Condyles.
Capt. Laman A. Gray, M. C., Treatment of Gonorrhea in the Female with Penicillin.
Dr. James A. Seaman, Springfield, Mass., Endocervicitis as a Factor in Urologic Infections.
Dr. Victor K. Allen, Tulsa, Okla., Perirectal Fistula as a Port of Entrance for Torula Encephalitis.
Dr. Murdock S. Equen, Atlanta, Ga., Magnetic Removal of Foreign Bodies from the Food and Air Passages Under Fluoroscopic Guidance.
Dr. Stuart C. Cullen, Iowa City, Use of Curare in Anesthesia.

Other features of the session will be a symposium on the essentials of medical education participated in by:

Dr. Edwin P. Lehman, Charlottesville, Cultural Values in Medical Education.
Dr. Jacques P. Gray, Richmond, Va., Undergraduate Curriculum in Medicine.
Dr. Hiram W. Kostmayer, New Orleans, Medical Education Above the Undergraduate Level.
Dr. Cornelius O. Bailey, Los Angeles, Postwar Medical Education.
Dr. Victor Johnson, Secretary, Council on Medical Education and Hospitals, American Medical Association, Chicago, Postgraduate Training After the War.
Miss Marion A. Murphy, librarian, Washington University School of Medicine Library, St. Louis, The Effects of the War on the Medical School Library.

During the meeting of the Southern Medical Association other groups holding sessions will be the southern branch of the American Public Health Association, the National Malaria Society, American Society of Tropical Medicine, American Academy of Tropical Medicine and the southern chapter of the American College of Chest Physicians. The thirtieth annual meeting and dinner for women physicians of the Southern Medical Association will be held November 15.

FOREIGN

Personal.—Dr. Alan N. Drury, director of the Lister Institute, London, has been named honorary secretary of the advisory board to the Beit Memorial Trustees, the group sponsoring the memorial fellowships for medical research.

Academy of Medical Sciences in Russia.—An Academy of Medical Sciences of the Union of Soviet Socialist Republics has been organized, the *British Medical Journal* reports. It is to be set up under the People's Commissar for Health and will have three departments: medical biology, hygiene, microbiology and epidemiology, and clinical medicine.

Deaths in Other Countries

Israel J. Kligler, Ph.D., formerly an associate of the Rockefeller Institute for Medical Research, died in Jerusalem, September 23. Dr. Kligler, who had held the Jacob Epstein chair of bacteriology and hygiene at Hebrew University since 1926, came to Palestine in 1943 as head of the malaria research unit sent by Hadassah the Zionist women's organization. Dr. Kligler, who was born in Austria in 1889, received his doctor of philosophy degree at Columbia University in 1915.

CORRECTION

Therapeutic Effect of Para-Aminobenzoic Acid in Louse Borne Typhus Fever.—In the paper by Yeomans et al. in THE JOURNAL, October 7, the authors request that the following correction be made in table 6 on page 354: The average age of the B group should be changed from 18 to 27.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Sept. 30, 1944.

Chair of Child Health Established in London

With Lord Nuffield's approval the trustees of the Nuffield Foundation have allocated $50,000 a year for ten years to provide a chair of child health in the University of London, an offer which has been gratefully accepted by the trustees of the university. This grant will enable a postgraduate institute of child health to be created for teaching and research on all aspects of child health. It is proposed that the institute shall be associated with the principal children's hospital in this country —the Hospital for Sick Children, Great Ormond Street, London, and with the obstetric department of the British Postgraduate Medical School at the Hammersmith Hospital. Lord Nuffield and the trustees of his foundation believe that the promotion of child health must have a prominent place in the organization of the future health services of the country. They appreciate that the development of research and training in this sphere requires new and enlarged facilities. They desire that the exceptional resources of the University of London for postgraduate education and research may be developed in a manner which will make the new Institute of Child Health worthy of the capital city of the empire.

The provision of academic centers for the teaching of child health has already been undertaken in several provincial universities, and the Nuffield Provincial Hospitals Trust has within the last three years made a substantial contribution to the University of Durham to assist in creating a chair of child health at King's College, Newcastle-on-Tyne. Edinburgh has had such a chair since 1931, and another has just been established at Liverpool by collaboration of the university with the city council. The title of the new chair is noteworthy. This country has never been backward in the study of pediatrics; on the contrary, it has made great advances in that subject. But "Hospital" or "Department for Diseases of Children" has always been the designation for the institution concerned. Now the idea has become popular that the medical profession has been too preoccupied with the treatment of disease, and that prevention, or the preservation of health, should have a more prominent place as an objective. Calling the government's projected scheme a "National Health Service" instead of a "National Medical Service" is a case in point.

The Doctor's View of the Proposed National Health Service

Under the caption "The Doctor's View," Lord Dawson, president of the British Medical Association, reviews the government's proposals for a national health service in a letter to the *Times*. The medical profession, he says, has realized that the growth of medical knowledge was outstripping the organization of medical practice and for nearly twenty-five years has put forward plans to improve the availability of its services. There is little dispute over objectives, then, but there are differences about methods. The profession insists on a substantial share in the planning and administration of the proposed service at every level, Lord Dawson states. The service should be guided by those persons, both medical and lay, who have expert knowledge. Do local authorities know anything about medicine? he asks. How can they plan and administer, unaided, hospital services? In the war we use expert guidance. Why attempt to do otherwise with medicine, which becomes more complex year by year?

We accept the proposal that this nationwide service, which spends public money, must be under the egis of a minister responsible to parliament, Lord Dawson says, but we claim also that, for the service to be efficient, the medical profession must have a responsible share in its planning and administration. To effect this at the center would be relatively easy if the two sides were like minded, but local administration has inherent difficulties, because its present shape and the proposed service would be misfits, it is claimed. Since the reconstruction of local government will be impossible amid pressing postwar problems and it is undesirable to delay laying the foundations of the service, it is acknowledged that we must seek a provisional, "make do" administration, provided skilled guidance is secured and provided the voluntary hospitals are ensured equality of opportunity and private practice is given full freedom. These requirements would be met if medical and other skilled persons were made partners with the elected representatives of the people on the local bodies. The profession seeks to share in, not to dominate, the work of planning and execution.

Experience has shown that advisory committees standing outside the executive body are futile, the letter continues. The inadequacy of local bodies, as now constituted, to administer highly technical services is well known. But extraneous forces obstruct satisfactory settlement. One political school desires to seize this opportunity for furthering its ideology, which would mean whole time employment for medical men as part of the civil service, paid by salary. The impact of this influence, in the face of the government's repeated assurance that it has no such intentions, undermines confidence, Lord Dawson points out. Regarding the voluntary hospitals, suggestions are being made to transfer the administration of all hospitals to a central board. These suggestions are unfortunate. It is most important to take advantage of the knowledge, interest and local patriotism of each area and put responsibility on it. Central control would take the heart out of local government and lead to inanimate uniformity. The smooth running of a coordinated hospital service for each area under university influence is the foundation of any comprehensive service, the president's letter concludes.

The Dalton Centenary

John Dalton, who founded modern chemistry by putting the atomic theory on a quantitative basis, worked in Manchester, where he taught mathematics and physics. He contemplated entering the medical profession, but the expense was too great. He had a defect of color vision, now known as "daltonism," which he turned to account by producing his theory on the subject. The centenary of his death has fallen this year. It is therefore fitting that a Manchester physician, Dr. E. M. Brockbank, who has made Dalton's life a study, has published a book entitled "John Dalton—Some Unpublished Letters of Personal and Scientific Interest with Additional Information about his Colour Vision and Atomic Theories." When the 1929 meeting of the British Medical Association was held at Manchester Dr. Brockbank, president of the Section of the History of Medicine, gave an address on "John Dalton—Experimental Physiologist and Would-Be Physician." He had access to Dalton's letters and other relics and has made a thorough study of the subject.

Research at Oxford and Cambridge by Chinese

Five Chinese professors have arrived in Britain and will be the guests of certain colleges of Oxford and Cambridge. Chang Tsu-King, professor of the history of science at the Central China University, will reside in Christ's College, Cambridge, to study that subject. Yin Hung-Chang, professor of plant biochemistry at the Associated Southwestern Universities (Tsing Hua), Kumming, will do research at St. John's College, Cam-

bridge. Fan Tsen-Chung, head of the foreign languages department at the National Central University, Shapingpa, will do research in English literature, with special reference to English knowledge of China, and reside at Balliol College, Oxford. Chang-Hui-Wen, head of the department of public administration and political science at the Central University of China, will study public administration at Corpus Christi College, Cambridge. R. C. Fang, head of the foreign languages department, Wuhan University, Kiating, will do research in English literature at Trinity College, Cambridge.

BUENOS AIRES

(From Our Regular Correspondent)

Sept. 15, 1944.

Quinine and Malaria

Quinine is available in Argentina in scanty amounts. It is sold to the public only for malaria therapy and when public health authorities approve its use for other purposes. The government recently appointed a committee, as a branch of the National Department of Public Health, for studying the possibilities of obtaining quinine substitutes. A fund of $15,000 was awarded for the studies. Drs. Carlos A. Alvarado, head of the National Antimalarial Department, Prudencio Santillan, secretary of the department, Cecilio Romano, head of the Instituto de Medicina Regional of the University of Tucumán, and Horacio Descole, head of the Lillo Institute of Tucumán, are the main members of the committee. The preliminary essays gave promising results. Further botanic and pharmacologic researches are progressing.

The government recently awarded $150,000 to the national department for expenses incurred in the antimalarial crusade in the central and northern regions of the country. Regulations for free distribution of antimalarial drugs and plans for the crusade were submitted to the government by Dr. Carlos A. Alvarado, head of the National Antimalarial Department, and were approved. A batch of 400 larvogenic fishes was recently sent to the National Antimalarial Department by the Rockefeller Institute.

Beta Vulgaris and Pollinosis

Drs. L. Herraiz-Ballestero and J. V. Monticelli recently lectured before the Argentine Society of Biology. They said that the coastal variety of Beta vulgaris grows abundantly near Bahia Blanca in Buenos Aires. The plant produces large amounts of pollen between October and December up to the end of the second week of December. Its pollen is the most frequent causal agent of pollinosis in the region, as shown by the results of skin tests, which were done on 150 patients with pollinosis. The pollinosis section of Bahia Blanca is heavily loaded with the pollen of Beta vulgaris, which fulfils Thommen's postulates. Pollinization of this chenopodiacea herb precedes or accompanies pollinization of gramineous plants. The fact is of importance, they said, especially in connection with therapy of the disease.

Brief Items

Pamphlets for education of the public on poliomyelitis are being distributed to the public by the government of Buenos Aires. The measures for preventing the disease are explained.

A celebration was held recently at the Faculty of Medicine of La Plata, which recently reached its twenty-fifth anniversary.

Drs. Armando Marotta and Nicanor Palacios Costa were recently appointed president and numeric member of the Academia Nacional de Medicina of Argentina. The library of the academy was officially opened on this occasion. It has more than 40,000 volumes.

Dr. Carlota Pereira de Queiroz of Rio de Janeiro recently delivered a lecture at the National Academy of Medicine of Buenos Aires. She spoke on the applications of hematologic examination to social medicine.

BELGIUM

(From Our Previous Correspondent)

Sept. 21, 1944.

Gratitude of the Belgians

The people of Belgium deeply appreciate the liberation of our country by the Allies. They have shown their patriotic enthusiasm for the cause of liberation and their admiration for your army. We, the Belgian physicians, wish to express also our deep gratitude to your country and our admiration for your army. We are now able to see for ourselves on our reconquered soil the amazing organization of war surgery that has been built up by the Allies at the front. Because of our experience with the hospitals during the war of 1914-1918 we can appreciate the progress achieved in the care of the wounded, and we propose to learn from contact with your medical officers the advances in war surgery that have given such good results in this war.

I wish to write a few words regarding our experiences during the occupation: The practice of all Belgian physicians was regulated by a dictatorial order which had many arbitrary rules (for authorization to practice, location of physicians and similar matters). Fortunately these regulations were received generally with inertia, and 90 per cent of physicians continued practicing without openly protesting against the regulations, suffering vexation, to be sure, but practically ignoring their existence.

As for the Belgian medical press, two journals continued to be published, one in Flemish and one in French. Some of the material of medical journals which were suppressed by the invaders was provisionally published by the International Office of Medico-Military publications in the *Archives médicales Belges* from May 10, 1940. We never could obtain any medical literature except from Germany. All papers were suppressed by the invaders. The literature that we received consisted of medical items from Swiss journals sent to us in envelops as if they were letters.

The nightmare is over now. The medical profession and the rest of the country are ready to resume their normal place in the world.

Marriages

ROBERT PAYNE BECKWITH JR., Roanoke Rapids, N. C., to Lieut. Nancy Margaret Kimbrough of Romney, W. Va., August 8.

WILLIAM FRANCIS KIELY, Birmingham, Ala., to Miss Margaret Helene McMenamin at San Francisco, September 25.

ARNOLD W. BROCKMOLE, Evansville, Ind., to Miss Martha Frances Jakubiak of St. Louis in Cleveland, September 9.

EUGENE LEONARD WATKINS, Worcester, Mass., to Miss Victoria Pauline Peake of Brooklyn, September 23.

EDWARD MORSE SHEPARD to Miss Elizabeth Wendell Yates, both of New York in Nantucket, Mass., September 5.

HUBERT J. THOMAS, Dallas, Texas, to Miss Joella Henderson of Burkett in Wichita Falls, July 12.

GEORGE F. MCAULIFFE, North Vernon, Ind., to Miss Sally C. Edelen of Bardstown, Ky., April 15.

LAURENCE BRUGGERS, St. Anne, Ill., to Miss Edith Lois Fuller of Amesbury, Mass., July 31.

IRVING E. BENVENISTE, Los Angeles, to Miss Angela Gower Cole of Minot, N. D., August 6.

GEORGE PLATT PILLING IV, Philadelphia, to Miss Barbara Bosworth of Denver, October 2.

FREDERICK YATES to Mrs. Lou E. Cunningham, both of Washington, D. C., September 9.

EUGENE B. BRODY, Columbia, Mo., to Miss Marian Holen of Evanston, Ill., recently.

RODNEY CHARLES TURNER, Norfolk, Va., to Miss Mary Anna Ayers, September 3.

LAWRENCE LIMBERT, Norristown, Pa., to Miss Lois Fisher of Harrisburg, July 5.

Deaths

Charles St. John Butler ✠ Medical Director, Rear Admiral, U. S. Navy, retired, Bristol, Tenn.; University of Virginia Department of Medicine, Charlottesville, 1897; entered the medical corps of the U. S. Navy as a lieutenant (jg) in 1900; advanced through the various grades to that of rear admiral in 1935; retired on April 1, 1939; instructor in bacteriology and tropical medicine intermittently at the U. S. Naval Medical School from 1907 to 1921 and commanding officer from 1921 to 1924 and from 1927 to 1932; formerly professor of tropical medicine at George Washington University School of Medicine, Washington, D. C., and Hahnemann Medical College and Hospital, Philadelphia; commanding officer, U. S. Naval Hospital, Brooklyn, from 1932 to 1935; director general of public health of the republic of Haiti from 1924 to 1927; commanding officer of the U. S. Naval Medical Supply Depot in Brooklyn, 1935-1936, and the U. S. Naval Medical Center in Washington from 1936 to 1938; detached March 31, 1939 as president of the naval retiring board and board of medical examiners and naval retiring board for officers of the medical corps; specialist certified by the American Board of Internal Medicine; served as a member of the medical board of the National Research Council, the Subcommittee on Medical Research, the National Malaria Committee, the National Advisory Health Council, the scientific board of the Gorgas Memorial Institute of Tropical and Preventive Medicine, the American Association for the Advancement of Science, the Washington Academy of Sciences, the American Association of the History of Medicine, the American Society of Clinical Pathologists and the Association of Military Surgeons of the United States; member and past president of the American Academy of Tropical Medicine, New York Society of Tropical Medicine, American Society of Tropical Medicine, the Washington branch of the Society of American Bacteriologists and the Helminthological Society of Washington; honorary member of the Society of Medicine, Haiti; fellow of the American College of Surgeons, American College of Physicians and the New York Academy of Medicine; decorated with the medal of honor and merit of Haiti; received a letter of commendation from the U. S. Navy Department for service in World War I; awarded the LL.D. degree by the Emory and Henry College in 1932; author of "Syphilis Sive Morbus Humanus"; died October 7, aged 69, of cerebral hemorrhage.

Edward Shearman McSweeny ✠ New York; Bellevue Hospital Medical College, New York, 1898; member of the American Association for Thoracic Surgery, American Association of Industrial Physicians and Surgeons, American Trudeau Society and the National Tuberculosis Association; fellow of the American College of Physicians; specialist certified by the American Board of Internal Medicine; formerly demonstrator of anatomy and lecturer on tuberculosis treatment and convalescent care at the New York University Medical College; formerly medical superintendent of the Sea View Hospital in Castleton Corners, N. Y., and the Tuberculosis Sanatorium of the New York City Department of Health in Otisville, N. Y.; served as medical director of the New York Telephone Company; for many years on the board of visitors of the New York State Hospital, Ray Brook; chairman of the medical board, Tuberculosis Preventorium for Children, Farmingdale, N. J.; consulting physician to the Grasslands Hospital, Valhalla, N. Y., Mary Immaculate Hospital, Jamaica, and St. John's Long Island City Hospital, Long Island City; served on the medical board of the Stony Wold Sanatorium, Lake Kushaqua, N. Y., Workmen's Circle Sanatorium, Liberty, N. Y., and the Sanatorium Gabriels in Gabriels; received the degree of doctor of public health from New York University in 1921; died September 17, aged 66, of coronary thrombosis.

William Bradley Breed ✠ Boston; Harvard Medical School, Boston, 1920; associate in medicine at his alma mater; member of the committee on publications, councilor and chairman of the war participation committee of the Massachusetts Medical Society; member of the New England Heart Association and the American Clinical and Climatological Society; fellow, regent and president of the board of governors of the American College of Physicians; associate editor from 1923 to 1937 and on the editorial board from 1937 to 1942 of the *New England Journal of Medicine*; specialist certified by the American Board of Internal Medicine; member of the honorary staff, House of the Good Samaritan; since 1920 on the staff and at his death member of the executive committee of the Massachusetts General Hospital; died in the Phillips House of the Massachusetts General Hospital August 21, aged 51, of carcinoma.

Jeremiah T. Simonson ✠ New York; New York Homeopathic Medical College and Hospital, New York, 1891; emeritus professor of pediatrics at his alma mater, now known as the New York Medical College, Flower and Fifth Avenue Hospitals; past president of the American Institute of Homeopathy; member of the American Academy of Pediatrics; specialist certified by the American Board of Pediatrics, Inc.; in 1941 received the gold certificate from his alma mater awarded to alumni who are still in active practice fifty years after graduation; consultant on the staffs of the Fitkin Memorial Hospital, Neptune, N. J., Metropolitan Hospital and the Yonkers General Hospital, Yonkers, N. Y.; consulting pediatrician to the Flower and Fifth Avenue Hospitals, where he died September 30, aged 74, of hypernephroma of the right kidney and coronary sclerosis.

Joseph Marshall Flint, New Haven, Conn.; Johns Hopkins University School of Medicine, Baltimore, 1900; for many years professor of principles and practice of surgery at the Yale University School of Medicine; at one time professor of anatomy at the University of California, San Francisco; fellow of the American College of Surgeons; served overseas during World War I; commander of the Yale University Medical Unit and later commanding officer of Mobile Hospital number 39; named liaison officer, American Expeditionary Forces; when he left the service had been cited for conspicuous and meritorious service and was decorated by the French government; formerly chief surgeon at the New Haven Hospital and the New Haven Dispensary; died in Seal Harbor, Maine, September 16, aged 72, of coronary embolism.

Robert Law Cunningham ✠ Los Angeles; Johns Hopkins University School of Medicine, Baltimore, 1907; clinical professor of medicine at the University of Southern California School of Medicine; specialist certified by the American Board of Internal Medicine; past president of the Clinical and Pathological Society, now the Los Angeles Academy of Medicine, Los Angeles Tuberculosis Association and the California Tuberculosis Association; fellow of the American College of Physicians; member of the American Trudeau Society and the National Tuberculosis Association; served on the staffs of the La Vina Sanatorium, La Vina, the Hospital of the Good Samaritan, Barlow Sanatorium and Children's and St. Vincent's hospitals; died September 10, aged 63, of coronary thrombosis.

Hugh Spencer McKeown ✠ New York; Baylor University College of Medicine, Dallas, 1922; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; specialist certified by the American Board of Ophthalmology; served as assistant clinical professor of ophthalmology at the Columbia University College of Physicians and Surgeons; police surgeon of Bronxville and Westchester County; attending surgeon at the Institute of Ophthalmology of the Presbyterian Hospital; chief of the ophthalmologic service, Lawrence Hospital, Bronxville; on the staff of the Vanderbilt Clinic; died in the Harkness Pavilion, September 14, aged 49, of coronary thrombosis.

Charles Henry Tilghman Lowndes ✠ Medical Director, Rear Admiral, U. S. Navy, retired, Durham, N. C.; University of Maryland School of Medicine, Baltimore, 1888; entered the medical corps of the U. S. Navy as an assistant surgeon on April 12, 1889; rose through the various grades to that of rear admiral in 1919; retired March 1, 1929 on own application after thirty years' service; formerly medical director of the Georgetown University Hospital, Washington, D. C.; author of "Reports on Results of Indian Conditions on Various Reservations"; died in the Naval Hospital, Bethesda, Md., September 25, aged 78.

Edward Luther Whitney ✠ Walla Walla, Wash.; Baltimore Medical College, 1895; served as president of the Walla Walla Valley Medical Society; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; formerly professor of physiologic chemistry at his alma mater and associate professor of physiologic chemistry, pharmacy and clinical pathology at the University of Maryland School of Medicine; member of the staffs of the Walla Walla General and St. Mary's hospitals; died September 13, aged 73, of bilateral hemiplegia.

Thomas Warren Allred ✠ Nephi, Utah; Northwestern University Medical School, Chicago, 1923; served as county and city physician; president and for many years a member of the county board of education; died in the Payson City Hospital, Payson, August 6, aged 57.

Alexander Locke Anderson, Wolfville, N. S., Canada; Long Island College Hospital, Brooklyn, 1898; practiced in Brooklyn for nearly forty years; died June 29, aged 70.

Louis Baer ✠ Philadelphia; Medico-Chirurgical College of Philadelphia, 1913; specialist certified by the American Board of Otolaryngology; served an internship at the Garretson Hos-

pital; on the staff of the Mount Sinai Hospital; died in the Pennsylvania Hospital August 4, aged 56.

Frederick Clifton Ballard ✠ Rushford, N. Y.; University of Buffalo School of Medicine, 1898; for many years county coroner; for more than twenty years on the board of education of Rushford, serving at one time as president; health officer and school physician; on the staff of the Genesee Country Memorial Hospital, Fillmore; died August 16, aged 68, of cerebral hemorrhage and cirrhosis of the liver.

Robert Lenox Barnes ✠ Columbus, Ohio; Starling-Ohio Medical College, Columbus, 1910; associate of the American College of Physicians; member of the American Heart Association, American Society for the Study of Arthritis and the Columbus Academy of Medicine; on the attending staff, Mount Carmel Hospital; died August 2, aged 58, of cerebral hemorrhage.

Philip John Bartle, Eugene, Ore.; Barnes Medical College, St. Louis, 1896; member and past president of the Oregon State Medical Society; past president of the Lane County Medical Society; member of the Pacific Northwest Medical Association; served as president of the Oregon Association of Hospitals; for many years on the staff of the Eugene Hospital and Clinic; died September 5, aged 70, of ruptured aortic dissecting aneurysm.

John A. Biever, Mount Joy, Pa.; College of Physicians and Surgeons, Baltimore, 1885; died August 27, aged 86, of carcinoma of the liver.

William Henry Blanchette ✠ Fall River, Mass.; Baltimore Medical College, 1896; served during World War I; major, medical reserve corps, U. S. Army, not on active duty; died August 1, aged 71.

Braxton B. Blount, Punta Gorda, Fla.; Louisville Medical College, Louisville, Ky., 1890; examiner for the local Selective Service Board; died August 14, aged 79.

Walter William Brand ✠ Toledo, Ohio; Jefferson Medical College of Philadelphia, 1894; fellow of the American College of Surgeons; honorary president of the Ohio Obstetrical Society; formerly health officer of Toledo; for many years on the staff of St. Vincent's Hospital; resigned as chief of staff in 1934 and as director of obstetrics in 1942 at the Women's and Children's Hospital, where he died October 2, aged 73, of cerebral thrombosis.

Henry George Crease ✠ Bakersfield, Calif.; Jefferson Medical College, Philadelphia, 1891; formerly owner of the Trinity Hospital; died August 15, aged 78.

Annie Sturges Daniel ✠ New York; Woman's Medical College of the New York Infirmary for Women and Children, New York, 1879; for more than sixty years a member of the staff of the New York Infirmary for Women and Children; on the editorial board of the *Medical Woman's Journal;* author of "A Cautious Experiment"; died August 10, aged 85.

Cyril Ostello Dozer, Roseville, Ohio; Eclectic Medical College, Cincinnati, 1919; member of the Ohio State Medical Association; vice president of the school board; served during World War I; on the staff of the Bethesda Hospital, Zanesville; died in the Good Samaritan Hospital, Zanesville, August 21, aged 50.

Vernon King Stevenson Earthman, Shelbyville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1893; member of the Tennessee State Medical Association; veteran of the Spanish-American War and World War I; on the staff of the Rutherford Hospital, Murfreesboro; died August 8, aged 72, of coronary occlusion.

Charles Edward Eaton, Stanwood, Wash.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1904; member of the Washington State Medical Association; served during World War I; died at Camano Island August 21, aged 69.

Frank George Engelhardt, Syracuse, N. Y.; Syracuse University College of Medicine, 1892; veteran of the Spanish-American War; died August 18, aged 73, of carcinoma of the esophagus and stomach.

Wallace J. French, Pike, N. Y.; University of Buffalo School of Medicine, 1884; member of the Medical Society of the State of New York; health officer of the town of Pike; on the staff of the Wyoming County Community Hospital, Warsaw; died August 30, aged 85, of cerebral hemorrhage.

Alphonse Paul Gagnon, Taunton, Mass.; Tufts College Medical School, Boston, 1921; member of the Massachusetts Medical Society and the American Society of Anesthetists, Inc.; served an internship at the Fall River City Hospital, Fall River; examining physician of Selective Service Board number 148; formerly tuberculosis diagnostician of the board of health and chief of the staff of the Bay View Hospital in Fall River; on the staff of the Morton Hospital, where he died August 2, aged 52.

Clarence William Graser, Buffalo; University of Buffalo School of Medicine, 1918; member of the Medical Society of the State of New York; died in the Millard Fillmore Hospital August 20, aged 48, of cirrhosis of the liver.

Edward Melvin Green ✠ Harrisburg, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1890; member of the American Psychiatric Association; fellow of the American College of Physicians; member, medical advisory board, Pennsylvania Selective Service; formerly on the staff of the Georgia State Sanitarium, Milledgeville; consultant in psychiatry and administration and for many years superintendent of the Harrisburg State Hospital; died September 30, aged 76.

Ralph Hagan, Los Angeles; University of Southern California College of Medicine, Los Angeles, 1895; formerly police surgeon; served during World War I; on the staff of St. Vincent's Hospital, where he died August 20, aged 72, of angina pectoris.

John Albert Hagemann ✠ Pittsburgh; Columbus Medical College, 1884; member of the American Academy of Ophthalmology and Otolaryngology; specialist certified by the American Board of Otolaryngology; formerly on the staff of the Pittsburgh Hospital; died July 15, aged 81, of pneumonia.

Thomas J. Heavey, Medway, Mass.; Middlesex College of Medicine and Surgery, Cambridge, 1922; member of the Massachusetts Medical Society; died August 7, aged 58.

Harry Joseph Hill, Waltham, Mass.; College of Physicians and Surgeons, Boston, 1910; formerly a medical missionary in China; served during World War I; at one time on the staff of the Northampton State Hospital, Northampton; a member of the staff of the Metropolitan State Hospital; died August 6, aged 59, of cerebral thrombosis, general arteriosclerosis and diabetes mellitus.

Thomas Milton Hood, Clarksburg, W. Va.; Jefferson Medical College of Philadelphia, 1880; honorary member and in 1905 president of the West Virginia State Medical Association; twice president of the Harrison County Medical Society; at one time assistant superintendent of the Weston State Hospital, Weston; on the staffs of the Union Protestant Hospital and St. Mary's Hospital; died, September 27, aged 91, of senility.

Lester Paul Hulick ✠ Mansfield, Ill.; St. Louis University School of Medicine, 1925; served an internship at the Missouri Baptist Sanitarium, St. Louis; on the staff of the John and Mary E. Kirby Hospital, Monticello; died, August 20, aged 45.

Elmer C. Huselton, Pittsburgh; Jefferson Medical College of Philadelphia, 1884; formerly on the staff of the old Allegheny General Hospital; died August 24, aged 84, of heart disease.

Leon Downie Jay ✠ Waverly, Iowa; State University of Iowa College of Medicine, Iowa City, 1910; fellow of the American College of Surgeons; on the staff of the St. Joseph Mercy Hospital; died August 8, aged 58, of cerebral hemorrhage.

William Robert King, Minneapolis; Harvard Medical School, Boston, 1917; served an internship at the Peter Bent Brigham Hospital, Boston; on the staff of the Abbott Hospital; died August 10, aged 54, of cerebral hemorrhage.

Silvanus B. Kirkpatrick, Taylor, Texas; Missouri Medical College, St. Louis, 1883; honorary member of the State Medical Association of Texas; died in the Stromberg Clinic and Hospital August 4, aged 92, of uremia.

Dantan Wyeth Landess, Port Allen, La.; University of Tennessee College of Medicine, Memphis, 1930; member of the Louisiana State Medical Society; served as health officer and coroner of West Baton Rouge Parish; a lieutenant colonel in the Louisiana State Guard, in which he had been commander of the seventh battalion; an organizer and past president of the Port Allen Lions Club; died in Our Lady of the Lake Sanitarium, Baton Rouge, August 21, aged 48.

Kevin David Lynch ✠ El Paso, Texas; Columbia University College of Physicians and Surgeons, New York, 1911; member of the American Urological Association; president-elect and formerly vice president of the Southwestern Medical Association; served in France during World War I; on the staffs of the Hotel Dieu, Sisters' Hospital, Providence Hospital and the Southwestern General Hospital; died June 2, aged 58, of hypertensive heart disease.

Horace Cuilford MacKerrow, Worcester, Mass.; Leonard Medical School, Raleigh, N. C., 1904; University of Bishop College Faculty of Medicine, Montreal, Que., Canada, 1905; died in the Palmer Memorial Hospital, Boston, August 14, aged 64, of metastatic adenocarcinoma from the biliary tract.

Rufus Henry Main, Barry, Ill.; Missouri Medical College, St. Louis, 1894; member of the Illinois State Medical Society and its "Fifty Year Club"; for eighteen years secretary of the Pike County Medical Society; for many years member of the school board; died August 20, aged 76.

Daniel Joseph Maloney, Waterbury, Conn.; New York University Medical College, New York, 1896; past president of the Waterbury Medical Association; on the staffs of the Waterbury and St. Mary's hospitals; died August 4, aged 77, of carcinoma of the stomach and general arteriosclerosis.

Herman Gustave Maul ⊕ Denver; Denver and Gross College of Medicine, 1910; Army Medical School, 1915; member of the American Roentgen Ray Society and the Radiological Society of North America, Inc.; formerly an officer in the medical corps of the U. S. Army; major, medical reserve corps, U. S. Army, not on active duty; died August 13, aged 57, of injuries received when caught by a power saw.

Caesar Peele McClendon, New Rochelle, N. Y.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1903; died in Wells, Maine, August 31, aged 68, of heart disease.

Joseph N. Moore, Marshall, N. C.; University of North Carolina School of Medicine, 1905; for many years county physician; served as a member of the board of directors of the Aston Park Hospital, Asheville; died August 21, aged 60, of chronic myocarditis and carcinoma of the prostate.

Andrews Rogers, Columbus, Ohio; Columbia University College of Physicians and Surgeons, New York, 1901; since 1943 professor emeritus of obstetrics at the Ohio State University College of Medicine, where he had been professor from 1916; specialist certified by the American Board of Obstetrics and Gynecology, Inc.; on the staffs of the Starling-Loving University Hospital, Mount Carmel Hospital, Franklin County Tuberculosis Hospital and the Grant Hospital; died August 6, aged 71.

Capt. Leo E. Apanasewicz
M. C., A. U. S., 1915-1944

Robert E. Ryle, Walton, Ky.; Starling Medical College, Columbus, 1896; member of the Kentucky State Medical Association; died August 30, aged 72, of myocarditis and arteriosclerosis.

John Gibson Sargent, Centralia, Wash.; State University of Iowa College of Homeopathic Medicine, Iowa City, 1908; died July 26, aged 68.

Henry Damon Smith ⊕ Sanford, Fla.; University of Alabama School of Medicine, 1912; twice president of the Seminole County Medical Society; died August 12, aged 54.

William S. Steele, Bluefield, W. Va.; Baltimore University School of Medicine, 1893; died August 20, aged 76, of hepatitis.

Charles Nicholas Stroube ⊕ Roachdale, Ind.; University of Louisville Medical Department, Louisville, Ky., 1897; died suddenly, September 17, aged 75, of coronary occlusion.

George Edwards Tooley, Seattle; Marion-Sims College of Medicine, St. Louis, 1901; member of the House of Delegates of the American Medical Association in 1908; formerly chief medical officer of the Veterans Administration Facility in Wichita, Kan., and on the staff of the Veterans Administration Facility in Lincoln, Neb.; served during World War I; died in August, aged 68, of myocardial infarct.

Herman Luther Tutwiler, Patterson, Va.; Medical College of Virginia, Richmond, 1900; member of the Medical Society of Virginia; formerly vice president of the McDowell (W. Va.) County Medical Society and member of the West Virginia state legislature; died July 29, aged 71

William Franklin Waggoner, Carrollton, Ill.; Barnes Medical College, St. Louis, 1903; member of the Illinois State Medical Society; on the board of the Boyd Memorial Hospital; died in Macon, Mo., July 14, aged 77.

Capt. Jacob T. Farris
M. R. C., U. S. Army, 1916-1944

Thomas Francis Welch, Hartford, Conn.; Georgetown University School of Medicine, Washington, D. C., 1904; member of the Connecticut State Medical Society; president of the Hartford Medical Society in 1932; served as a member of the draft board of Hartford during World War I; member and past president of the staff of St. Francis Hospital; died July 19, aged 71, of cerebral thrombosis.

Cephas John Wells ⊕ Bartlesville, Okla.; Louisville Medical College, 1894; died September 9, aged 79, of congestive heart disease.

James Alexander White, Alexandria, La.; College of Physicians and Surgeons, Baltimore, 1892; member of the Louisiana State Medical Society; member of the board of directors and treasurer of the Louisiana College, Pineville; on the staff of the Baptist Hospital; died May 23, aged 76, of coronary thrombosis.

James Johnston Withers, Davidson, N. C.; Jefferson Medical College, Philadelphia, 1909; served during World War I; formerly a druggist; on the visiting staff of the Lowrance Hospital, Mooresville; died July 30, aged 64, of coronary occlusion.

KILLED IN ACTION

Leo Edwin Apanasewicz, Cleveland; St. Louis University School of Medicine, 1941; served an internship at St. John's Hospital; began active duty as a first lieutenant in the medical corps, Army of the United States, on July 25, 1942; later promoted to captain; served in the North African and Italian campaigns; died in an army hospital in England, June 15, aged 28, of wounds received in Normandy on D day, June 6.

Jacob Thomas Farris, Richmond, Ky.; Vanderbilt University School of Medicine, Nashville, Tenn., 1940; served an internship in pediatrics at the Strong Memorial Hospital and the Rochester Municipal Hospital, Rochester, N. Y.; commissioned a first lieutenant in the medical reserve corps of the U. S. Army in June 1940; began active duty on Aug. 25, 1941; promoted to captain in January 1943; stationed at hospital in Fort Knox, Kentucky, for one year and trained in various other posts in the U. S. Army before going overseas early in January 1944; landed with the invasion troops in Normandy on D day; twice cited for bravery and awarded the Silver Star; killed in France by shrapnel severing his spinal cord August 3, aged 27.

Bureau of Investigation

DANGEROUS TO HEALTH

Because of Inadequate Warnings on Labels

[Editorial Note.—These abstracts concern preparations which were specifically declared by the Food and Drug Administration of the Federal Security Agency to be misbranded because their labels failed to carry adequate warnings against giving them to children, or using them in the pathologic conditions in which they might be dangerous to health, or to caution against unsafe dosages or methods or duration of administration or application, for the protection of the user. The abstracts that follow are given in the briefest possible form: (1) the name of the product; (2) the name of the manufacturer, shipper or consigner; (3) the date of shipment; (4) the composition; (5) the type of nostrum; (6) the reason for the charge of misbranding, and (7) the date of issuance of the Notice of Judgment.]

Aurofectol, Purpoil No. 22 and Purpoil No. 600.—Purpoil Laboratories, Inc., Baltimore. Shipped March 9 and 25, 1942. Composition: Aurofectol essentially a mixture of oils and phenols. Purpoil Nos. 22 and 600 both essentially mineral oil with small quantities of iodine, chlorobutanol and menthol. Aurofectol adulterated because strength differed from that which label represented it to possess, since it was not an antiseptic. Misbranded because label falsely represented that product would be efficacious in treating dermatitis, eczema, acute catarrhal inflammation of tympanic membrane, acute and chronic infections of external auditory canal, acute myringitis and catarrhal otitis media; that it was an effective parasiticide and antiseptic in skin diseases and would produce desired results in treating infections of the skin of the external auditory canal. Purpoil products misbranded because labels failed to warn adequately against use by children or in those conditions wherein products might be dangerous to health, since frequent or excessive use might cause injury to the lungs. Purpoil No. 22 further misbranded because label falsely suggested that product was an effective treatment of acute and mild chronic infections of the nose, would cause a depletion of the swollen mucous membrane, promote drainage, greatly improve ventilation and gradually diminish excess discharge, regardless of its cause. Both Purpoil products also misbranded because falsely represented to have bacteria-destroying properties equivalent to phenol in the same strength and in the same type of oil. Purpoil No. 600 specially misbranded because of false statement, "Used in the treatment of chronic suppurative infections of the nose."—[*D. D. N. J., F. D. C. 759; September 1943.*]

Luebert's Iron Tonic Compound Tablets.—A. G. Luebert, Wilmington, Del. Shipped May 17 and June 27, 1941. Composition: essentially salts of iron and manganese, strychnine sulfate, arsenic trioxide, a phosphide, and fish oil. Misbranded because label failed to warn against giving product to children and elderly persons, in view of strychnine content, or to caution against taking more than the recommended dose, and against frequent or continued use because of strychnine and arsenic content; further misbranded because of label misrepresentation that product would produce rich blood, good health, strong nerves and astounding vitality, give strength and vigor to the entire system, cleanse the blood after accumulations of winter months, benefit the weak, run-down or depressed, produce proper activity of all organs and functions of the body, stimulate the nutritive functions, tone the digestive tract and benefit those conditions which call for an effective tonic, such as loss of appetite and a tired, run-down feeling. Further misbranded because of false representation that these tablets were solely an iron tonic, since they contained some additional drugs that were physiologically active; also misbranded because label failed to declare quantity or proportion of strychnine sulfate and arsenic trioxide.—[*D. D. N. J., F. D. C. 754; September 1943.*]

Pond's Digestans and Pond's Laxative Pills.—Pond Pharmacal Company, Inc., New York. Shipped Oct. 8 and Nov. 13, 1941. Composition: Digestans essentially sodium bicarbonate, peppermint oil, strychnine sulfate and extracts of laxative plant drugs, including aloin; Laxative Pills, essentially laxative plant drugs (including aloin and podophyllin) and small amounts of belladonna. Both articles misbranded because directions for use were inappropriate and inadequate for a laxative, since they provided for continued administration, which might establish the laxative habit; further misbranded because, though label cautioned user against taking laxatives in the presence of nausea, vomiting and abdominal pain, it failed to warn that such symptoms may be those of appendicitis; also misbranded because tablets contained strychnine but labeling failed to warn that not more than the recommended dosage should be taken and that use by children and elderly persons might be especially dangerous; misbranded further because warnings required by law were not conspicuous on the label. Misbranded again because of certain label misstatements regarding the action of ingredients of Digestans and because the Laxative Pills were not properly labeled as to active ingredients and quantity of contents.—[*D. D. N. J., F. D. C. 764; September 1943.*]

W. K. Sterline's Compound.—Webster K. Sterline, trading as W. K. Sterline, Sidney, Ohio. Shipped Dec. 30, 1940. Composition: alcohol by volume, 5.56 per cent, and in each fluid ounce 15.25 grains of potassium iodide and 14.46 grains of sodium bromide. Misbranded because label failed to bear adequate warnings against giving to children or taking it in those pathologic conditions wherein it might be dangerous to health, or against unsafe dosage, since, because of presence of potassium iodide, it should not be taken in cases of lung disease, chronic cough or goiter, and should be discontinued if a skin rash should appear; frequent or continued use might lead to mental derangement, skin eruptions or other serious effects. Also dangerous to health because, considering presence of sodium bromide, product should not be used by those suffering from kidney disease. Misbranded, also, because labels failed to state that product should not be administered to children under 6 years of age, and because they falsely declared the amounts of alcohol, potassium iodide and sodium bromide present.—[*D. D. N. J., F. D. C. 806; December 1943.*]

STIPULATIONS

Agreements Between Federal Trade Commission and Promoters of Various Products

Following are abstracts of stipulations in which promoters of "patent medicines," medical devices and cosmetics have agreed, following action by the Federal Trade Commission, to discontinue certain misrepresentations in their advertising. These stipulations differ from the "Cease and Desist Orders" of the Commission in that such orders definitely direct the discontinuance of misrepresentations. The abstracts that follow are presented primarily to illustrate the effects of the provisions of the Wheeler-Lea Amendment to the Federal Trade Commission Act on the promotion of such products:

Casafru.—In February 1944 Leo J. Dunn, trustee, trading as Mason Drug Company, Boston, entered into a stipulation with the Federal Trade Commission regarding this product. In this he agreed to discontinue any advertisement which did not reveal that Casafru should not be taken when abdominal pain, nausea or other symptoms of appendicitis are present. It was provided, however, that future advertisements need contain only the statement, "Caution: Use Only as Directed" if the instructions for use on the label should contain a warning to the same effect.

Dr. Edgar Health Shoes and Dr. Edgar Health Cushion Shoes.—In March 1944 A. J. Schoenecker and Margaret Wehse, co-partners trading as A. J. Schoenecker Shoe Company, Milwaukee, stipulated with the Federal Trade Commission that they would no longer use the descriptions "Dr. Edgar Health Shoes" and "Dr. Edgar Health Cushion Shoes" in advertising, branding or labeling the shoes that they sell, or the word "Doctor" or its abbreviation, either alone or with the word "Health," so as to imply that their shoes have been made in accordance with the design, or under the supervision, of a physician, or contain special scientific, orthopedic or health features which are the result of medical determination or services. They further agreed to discontinue representing, through use of the word "Manufacturers," that they make the shoes that they sell, or own and operate or directly and absolutely control the factory in which their shoes are made.

Hennafoam Shampoo.—This is put out by Alfred Horowitz, trading as Hennafoam Shampoo Company, New York City. In February 1944 he stipulated with the Federal Trade Commission that he would cease representing that the product has been tested, or tested and approved by Good Housekeeping Magazine or any other organization which it owns or controls, unless the tests have been made in such manner as to give reasonable assurance of its quality, nature and properties in relation to its intended use and to the fulfilment of the claims made for it.

Kondremul with Non-Bitter Extract of Cascara and Kondremul with Phenolphthalein.—These are products of the E. L. Patch Company, Boston. In February 1944 this concern entered into a stipulation with the Federal Trade Commission to discontinue any advertisement which did not reveal that the preparations should not be used when abdominal pain, nausea or other symptoms of appendicitis are present. It was agreed, however, that it would be sufficient for future advertisements to contain the statement, "Caution: Use Only as Directed" if and when the directions for use on the labels should carry a warning to the same effect.

Lashgro.—This is promoted by Beatrice Kornstein, trading as Avalon-Lane Company, New York. In February 1944 she stipulated with the Federal Trade Commission that she would cease representing, by use of the trade name "Lashgro" or otherwise, that her product causes the eyelashes to grow longer or thicker, will promote or in any way affect their growth, or correct or remedy red, scaly eyelids.

Stevens' Mineral Water, Stevens' Concentrated Mineral Water, and Stevens' 50-50 Water.—These were the subjects of a stipulation entered into with the Federal Trade Commission in March 1944 by E. A. Stevens of Dawson Springs, Ky., in which he agreed to discontinue the following misrepresentations in the advertising: That these waters are an effective treatment or relief for stomach trouble, acute or chronic nephritis, uremia, engorged liver or kidneys, rheumatism, gout, gallstones, dropsy, appendicitis and some other ailments; that the waters are a cure for chronic constipation or a treatment for that condition in excess of temporarily relieving it, or that the physiologic effects of the preparation are greater than those of a saline laxative and a weak antacid. He further agreed to discontinue any advertisement which represented that the use of these waters was safe, or which failed to reveal the potential danger in using them when abdominal pains, nausea or other symptoms of appendicitis are present. The stipulation provided, however, that when the potential danger in their use was noted on the label, the advertisement need contain only the warning, "Caution: Use Only as Directed."

Correspondence

POWDER FOR SURGICAL GLOVES

To the Editor:—An editorial in THE JOURNAL, September 23, entitled "Exit Talcum from the Surgical Scene" has provoked considerable comment among industrial hygienists. There you make the statement that "These lesions [the talc granulomas] are permanent because the body does not have adequate reparative power against talcum, which is essentially a silicate and which therefore induces a silicosis."

I would question the validity of the assumption that a silicate can cause silicosis, and several people have already written me to protest against your generalization. All experimental evidence derived from study of pure silicates indicates that as a class these minerals do not dissolve within the body to liberate their component silica with resultant fibrosis. In fact, most of the silicates are inert materials and only a few of them, like asbestos and possibly mica, may be irritating because of peculiar physical properties. These experimental results, based on the study of pure minerals, are not always applicable to the mixtures encountered in industry. Many dusts are named for their major component but analysis reveals that they contain significant quantities of quartz that may be responsible for pulmonary reactions noted in chest roentgenograms.

In the case of talc I know that contamination with quartz is responsible for some of the alleged reactions in the lungs. In other instances nomenclature is at fault and the inhaled minerals actually consist of mixtures of tremolite, anthophyllite (both fibrous silicates), serpentine and either granular or fibrous talc. The fibrous minerals produce the peculiar bodies found in asbestosis and, in my opinion, pulmonary reaction to these so-called "talcs" is due to their fibrous structure rather than to their silica content. They produce granulomas only when the particles are fairly large, 20 microns or more in length. Grinding them to 3 microns or less in maximum diameter renders them comparatively inert, so that tissue reaction is limited to simple phagocytosis. With crystalline silica, whose action is known to be chemical, the reverse is true and the finer the quartz the more irritating it becomes.

The talcum powder granulomas of the peritoneal cavity are obviously foreign body tubercles, for all observers have mentioned the detection of refractile mineral particles. The size of these particles is not usually mentioned, but they must obviously be quite large to be detected under the biologist's polarizing microscope. Petrographic examination of one commercial talcum for hospital use revealed particles and fibers ranging in size from 150 microns downward. This material consisted of fibrous tremolite and particulate talc, dolomite and serpentine. Other samples contained varying amounts of quartz. Experiment demonstrates that intraperitoneal injection of the untreated powder will produce foreign body tubercles; after regrinding to size 3 microns and under (the size at which quartz exerts its specific effects) intraperitoneal reaction is limited to phagocytosis. Fibrosis develops only about large accumulations of the powder, and this is a nonspecific reaction against the mass of foreign body. Regardless of particle size, reactions to talc are not progressive.

For the reasons cited I cannot subscribe to your explanation of the talc granuloma. "Reparative power" is involved only in the sense that the tissues have walled off an insoluble foreign body; I can discover no reason for considering such reaction an attempt to repair a chemical injury. The hypothesis that body fluids attack silicates and leach out the bases to leave silica in active form finds no support in controlled experimental observation.

LEROY U. GARDNER, M.D., Saranac Lake, N. Y.
Director, Saranac Laboratory for Study of Tuberculosis.

To the Editor:—I have been much interested in the discussion going on for some time about a substitute for talcum powder in operating room gloves.

Why do we need any substitute? If gloves are dry and hands are dry, as they should be, and the gloves are the right size, any foreign material unnecessarily introduced into the field is an added danger. I have been wearing rubber gloves in the operating room for over forty years and have never used any kind of glove powder. In these days of constantly changing operating room nurses I have to be on the alert to escape the avalanche of talcum with which I am constantly threatened, but so far I have valiantly held my ground and have gone into the operating room with fingers that are cleaner and have a better tactile sense.

This tendency to get rid of an evil thing by substituting another evil thing is a common fault in everyday thinking. There is no need to have a substitute for a nuisance.

DANIEL THOMAS QUIGLEY, M.D., Omaha.

"GETTING PATIENTS OUT OF BED EARLY IN THE PUERPERIUM"

To the Editor:—On page 839 of THE JOURNAL of July 22 Dr. Morris L. Rotstein of Baltimore makes the statement that during the blitz of 1940-1941 London maternity patients delivered in hospitals were allowed up a day after labor and sent home on the second or third day post partum. He adds that "no ill effects resulted from this mode of treatment."

It would seem that Dr. Rotstein is under some misunderstanding, for although one half of the institutional confinements in London take place in hospitals directly under my control and I am in close touch with the voluntary hospitals responsible for the remaining institutional births in London, I have never heard of such a routine. The true facts may interest your readers. During the whole war period, all expectant mothers who could be persuaded to leave London were evacuated at the eighth month to country maternity homes organized by the Ministry of Health and there they were retained until the usual fourteen days after confinement. At the end of this period they were discharged to country billets with their infants, but many returned soon after to their homes in London, especially if the blitz was not active.

Of the mothers who could not be persuaded to leave London, those who were normal medically and whose homes were suited for confinements were expected to have their babies at home. This is the usual prewar custom in England, and we did not depart from it during the blitz, but of course enemy action rendered many houses unsuitable and added to the pressure on our beds. Further, all hospitals retained the fourteen day period during the early part of the war, but many (including the London County Council's hospitals) were obliged to reduce the mothers' stay to ten or twelve days as accommodation was reduced by bombing or by necessary air raid precautions. Any woman who had to be sent home earlier (which very rarely happened and never before the seventh day) was conveyed by ambulance and a visiting nurse was sent to care for her. It is also true that in two areas of London where hospital accommodation became very short the women were (and are still) transferred by ambulance to a suburban hospital with excellent accommodation on the fourth day, but they are not expected to go home till the twelfth day. No bad effects have been reported, but the arrangement is much disliked by the women and will be abandoned directly events permit. It is probably a garbled version of this plan which has reached Dr. Rotstein.

May I add that we have had many attempts in the last forty years to introduce a shortened puerperium into English mid-

wifery practice but they have never taken hold. The present tendency is to insist more firmly than ever on six to seven days in bed and a total fourteen days of rest and exemption from household duties, with a longer convalescence still after complicated confinements. The value of graduated physical exercises during the antepartum period and from the third or fourth day of the puerperium is of course widely appreciated.

ALLEN DALEY, M.D.,
Medical Officer of Health, London County Council.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Chiropractic Practice Acts: Revocation Proceedings Not Barred by Failure of the Licentiate to Renew License.—The state of Iowa in February 1943 instituted proceedings to revoke Otterholt's license to practice chiropractic in Iowa, charging that the chiropractor was guilty of wilful and repeated violations of the Iowa laws relating to the practice of the healing arts. It was alleged that the chiropractor had repeatedly not confined his practice to chiropractic and had treated his patients "with electric and other machines, which is not the proper practice of chiropractic but is the practice of medicine and surgery for which he has no license." It was also alleged that the chiropractor was guilty of fraud and misrepresentations as to his skill and ability "in using a machine termed a 'Pathoclast' of no therapeutic value and falsely representing its therapeutic value." The chiropractor moved to dismiss the action, questioning the authority of the state to institute the action and the constitutionality of the state laws relating to the healing arts. Under the applicable Iowa law every license to practice a profession expires annually on the 30th day of June but can be renewed without examination on application accompanied by the legal fee at least thirty days prior to the expiration of the license. The chiropractor permitted his license to expire and did not apply for a renewal thereof. Subsequently he amended his motion to dismiss and contended that since he no longer was licensed to practice the action should be dismissed because the question of cancellation of his license was now moot. The trial court sustained the motion "on ground that cause of action has ceased to exist." The state accordingly appealed to the Supreme Court of Iowa.

The chiropractor, said the Supreme Court, had the right to practice chiropractic by virtue of the license granted by the state, acting under its police power. Such practice involves the health and safety of the citizens of the state, and practice under such license is subject to all reasonable conditions and regulations. Among such conditions is the requirement of annual renewal. This court on many occasions has sustained the right of the state to regulate the practice of the healing art and the constitutionality of the laws on the subject now in force. Through the license to practice granted the chiropractor by the state, subject to the regulations referred to, the chiropractor is the possessor of a valuable privilege or right, "which cannot be denied or abridged in any manner except after due notice and a fair and impartial hearing before an unbiased tribunal." *Gilchrist* v. *Bierring*, 14 N. W. (2d) 724. "The state cannot by issuing only annual licenses ingeniously thwart those precious rights," and "once an annual license is issued to a [licentiate] unless he has violated some of the provisions of the statute applicable to his profession he is entitled to the renewal of his license as a matter of right."

The Supreme Court did not agree with the holding of the trial court that the cause of action against the chiropractor had ceased to exist when the chiropractor failed to renew his license. There is a marked difference, said the court, between a license to practice a profession and a mere renewal of that license. As was said by this court in *Gilchrist* v. *Bierring*, supra:

> This is because a dentist, doctor, lawyer or the member of any other profession does not devote the years of study and preparation necessary to qualify as a practitioner merely that he may be accorded the right to practice for one year. When he qualifies for the practice, he does so for life. That right cannot be taken from him except by due process of law.

The certificate entitling the chiropractor to practice is a finding by the duly constituted authority that he has the necessary character and qualifications to practice chiropractic. The mere failure to renew annually does not lessen the value of that license except for the lapsed period before the renewal. The chiropractor is still the owner of the license and may be reinstated and continue the practice of chiropractic without examination, subject, as always, to the supervisory power under which he previously exercised it, such right to practice being evidenced by its renewal. All benefits of his license did not expire on July 1, 1943. His rights under the original license are of value. To deprive him absolutely and finally of the right ever to practice is much more serious than the mere suspension of that right, either voluntary or compulsory. Contrary to the procedure in renewal, in which one who is not an offender against the rules regulating the practice is entitled to a renewal as a matter of right, one who has had his license revoked must commence anew by making an original application for another license. *Hanson* v. *State Board of Medical Examiners*, 220 Iowa 357, 260 N. W. 68.

We do not consider the question involved moot, merely because the chiropractor is not at present making full use of his license to practice. As stated in 3 American Jurisprudence 366:

> It may be noted that the question whether a provision in a decree confers a particular right upon a party is not rendered moot on appeal merely because such party testified at the trial that he did not expect to exercise such right.

To hold otherwise places in the hands of the accused practitioner himself the power to escape the penalty provided by law for a violation of the rules governing the conduct of his practice, no matter how gross his misconduct may have been. The cause of action has not ceased to exist so long as there remain rights undetermined and all matters involved in the action have not been adjudicated. We are satisfied that the cause of action has not ceased to exist.

The Supreme Court accordingly ordered the cause to be returned to the trial court for trial on the merits.—*State v. Otterholt, 15 N. W. (2d), 529 (Iowa, 1944).*

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

BOARDS OF MEDICAL EXAMINERS
BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, Oct. 21, page 515.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Various centers, Nov. 13-15. Part III. Various centers, October. Exec. Sec., Mr. E. S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: New York, June 8-9. Final date for filing application is March 12. Sec., Dr. George M. Lewis, 66 E. 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Feb. 19. Final date for filing application is Dec. 15. Asst. Sec., Dr. W. A. Werrell, 1301 University Ave., Madison 5, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Spring 1945. Final date for filing application is Feb. 1. Sec., Dr. Paul C. Bucy, 912 S. Wood St., Chicago 12.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written. Part I.* Various centers, Feb. 3. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh 6.

AMERICAN BOARD OF OPHTHALMOLOGY: New York, June, Chicago, October, 1945. Final date for filing application is Dec. 1. Sec., Dr. S. Judd Beach, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF PEDIATRICS: *Oral.* New York, April 14-15. Final date for filing application is Dec. 15. Chicago, May 19-20. Final date for filing application is Jan. 19. Sec., Dr. C. A. Aldrich, 115½ First Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral.* New York, June 3. Final date for filing application is May 1. Sec., Dr. B. R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1934 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Heart Journal, St. Louis

28:133-268 (Aug.) 1944

Measurements of Circulation in Patients with Multiple Arteriovenous Connections. J. A. Kennedy and C. S. Burwell.—p. 133.
Fusion Beats and Their Relation to Syndrome of Short PR Interval Associated with Prolonged QRS Complex. J. S. Butterworth and C. A. Poindexter.—p. 149.
On Apical Sounds and Murmurs in Aortic Regurgitation. A. A. Luisada.—p. 156.
Unusual Effect of Interpolated Ventricular Premature Systoles. L. N. Katz, R. Langendorf and S. L. Cole.—p. 167.
Relation of Neurocirculatory Asthenia to Graves' Disease. E. Moschcowitz and S. S. Bernstein.—p. 177.
Further Observations on Deep Q_3 of Electrocardiogram. Annie Mary Lyle.—p. 199.
Peripheral Blood Flow and Other Observations in Coarctation of Aorta. H. J. Stewart, Helen S. Haskell and W. F. Evans.—p. 217.
*Differentiation of Electrocardiographic Changes Produced in Dog by Prolonged Temporary Occlusion of Coronary Artery from Those Produced by Postoperative Pericarditis. R. H. Bayley and J. S. La Due.—p. 233.
Effect of Dehydration Produced by Mercupurin on Plasma Volume of Normal Persons. R. H. Lyons, N. L. Avery and S. D. Jacobson.—p. 247.

Electrocardiographic Changes in Coronary Occlusion and Postoperative Pericarditis.—Bayley and La Due describe experiments on dogs which were devised to test the interpretation offered by Blumgart and his co-workers concerning the "prolonged" electrocardiographic changes associated with experimental temporary occlusion of a coronary artery. The authors present a method by which the electrocardiographic changes due to experimental coronary occlusion may be differentiated from those caused by the associated postoperative pericarditis. They show that the changes in the final ventricular deflections which are due to experimental temporary coronary occlusions of fifty minutes or less vanish completely within thirty minutes after cessation of occlusion and that the changes which appear on and after the first postoperative day are caused by local postoperative pericarditis. The duration of the electrocardiographic changes which immediately follow cessation of occlusions of fifty minutes or less is directly proportional to the duration of the occlusion. There are no differences in the magnitude or in the kind of electrocardiographic changes which are produced by acute local ventricular ischemia and injury, on the one hand, and by local postoperative pericarditis, on the other. The former occur during and for a brief time after temporary occlusion. For the most part the latter occur on and after the first postoperative day. The site of generation of the electrical effect which account for the two etiologically different groups of changes is different, i. e. the electrical effects associated with occlusion are generated in the muscle ordinarily irrigated by the occluded artery, whereas those associated with postoperative pericarditis are generated by the muscle adjacent to the local epicarditis which results primarily from the trauma of dissection of the coronary artery and from the trauma caused by the sutures which are used to close the pericardial sac. These observations differ decidedly from those of Blumgart and his co-workers. The authors ascribe the differences to the use by the other investigators of extremity leads only. It is important not to rely entirely on extremity leads for an evaluation of the electrocardiographic changes which occur in association with animal experimentation.

American Journal of Medical Sciences, Philadelphia

208:141-280 (Aug.) 1944

Use of Gelatin Solutions in Treatment of Human Shock. D. D. Kozoll, H. Popper, F. Steigmann and B. W. Volk.—p. 141.
Increases in Plasma Volume Following Administration of Sodium Salts. R. H. Lyons, S. D. Jacobson and N. L. Avery.—p. 148.
Orientation of Army Psychiatrist. P. Haun.—p. 154.
Convulsive Shock Therapy in Involutional States After Complete Failure with Previous Estrogenic Treatment. A. E. Bennett and C. B. Wilbur.—p. 170.
Endocrine Factor in Homosexuality: Report of Treatment of 4 Cases with Androgen Hormone. L. A. Lurie.—p. 176.
*Sulfamerazine (2-Sulfanilamido-4-Methylpyrimidine): II. Sulfonamide Concentrations in Blood of Man Produced by Small, Daily, Oral Doses of Sulfamerazine, Sulfamethazine, Sulfadiazine and Sulfathiazole. A. D. Welch, P. A. Mattis, E. S. Koelle and A. R. Latven.—p. 187.
Studies on Bone Marrow in Vitro: II. Effect of Hemoglobin and Red Cell Stromata on Explanted Bone Marrow. M. Rachmilewitz and A. Rosin.—p. 193.
Cardiac Arrhythmias in 1,000 Cases of Pulmonary Tuberculosis. T. T. Fox and A. L. Bobb.—p. 201.
*Significance of Marked Left Axis Deviation of Electrocardiogram. J. M. Faulkner and C. N. Duncan.—p. 205.
Development of Hypertension Associated with Lesions of Kidney. H. O. Mosenthal.—p. 210.
Studies on Morphology of Adrenal Cortex and on Excretion of 17-Ketosteroids in Hypertensive Patients. M. Bruger, J. A. Rosenkrantz and B. E. Lowenstein.—p. 212.
Factors Influencing False Positive Serologic Reactions for Syphilis Due to Smallpox Vaccination (Vaccinia). G. O. Favorite.—p. 216.
Phosphorus Poisoning: Report of 16 Cases with Repeated Liver Biopsies in Recovered Case. J. S. LaDue, J. R. Schenken and L. H. Kuker.—p. 223.
Acute Meningococcal Encephalomyelitis. W. B. Wartman and I. C. Hanger.—p. 234.
Mumps Epidemic in Small Task Force. H. Dermon and E. W. LeHew.—p. 240.

Sulfonamide Concentrations in Blood.—The experiments by Welch and his collaborators were designed to compare concentrations of sulfonamide produced in the blood of normal human subjects by daily administration of a single small dose of sulfamerazine, sulfadiazine, sulfamethazine or sulfathiazole. Observations were made on the average sulfonamide concentrations produced in the blood of 8 normal men by daily 1 Gm. doses of these drugs. The concentration in the blood following maintenance doses of sulfamerazine fell from a daily maximal value of about 6.5 to a minimal value of about 3.5 mg. per hundred cubic centimeters, with sulfadiazine from about 3.5 to about 1.5, with sulfamethazine from about 4 to less than 1, and with sulfathiazole from about 2 to less than 1 mg. per hundred cubic centimeters. Sulfamerazine administered in single 0.5 Gm. daily doses maintained a concentration in the blood which fell gradually from a level of approximately 4 to a level of about 2 mg. per hundred cubic centimeters. Emphasis is placed on the rapid absorption and gradual elimination of sulfamerazine, which make possible the maintenance of a concentration in the blood, with single daily doses of only 0.5 to 1 Gm., that is probably sufficient for certain chemoprophylactic purposes. The data presented, as well as clinical experience with sulfamerazine, indicate that adequate therapeutic concentrations in the blood should be maintained by the administration of smaller total daily doses than with other sulfonamides; these doses can be given on the basis of only two or three divided doses daily.

Significance of Great Left Axis Deviation.—While it is generally recognized that moderate deviation of the electrical axis of the heart to the left is a common finding in normal persons, its frequency approximating 20 per cent, there appears to be little agreement as to the significance of the less frequent but by no means rare pattern of great left axis deviation in which S_2 is of greater amplitude than R_2. Faulkner and Duncan studied clinical records of 200 consecutive cases exhibiting this pattern. The records revealed that 51.5 per cent had no left ventricular enlargement. Measurements of the heart from teleroentgenograms in 97 cases were within normal limits in 35. The heart was normal anatomically in 8 of 27 cases subjected to necropsy. There was a definite increase in the incidence of the pattern in the older age groups. The authors conclude that great left axis deviation in an otherwise normal electrocardiogram is a normal variation which, though encountered with increasing frequency with advancing age, cannot be correlated with ventricular enlargement, coronary disease or myocardial disease.

American J. Obstetrics and Gynecology, St. Louis

48:149-298 (Aug.) 1944. **Partial Index**

Pelvic Model Manikins to Show Pelvic Shape and to Demonstrate Labor Mechanisms. H. C. Moloy.—p. 149.
Herpes Gestations, with Report of 2 Cases and Survey of Literature. C. W. Mueller and W. A. Lapp.—p. 170.
Oral Substitution Therapy with Ethinyl Estradiol and Alpha Estradiol. F. E. Harding.—p. 181.
Hysterosalpingography, Routine Aid in Gynecologic Diagnosis. P. Bernstein.—p. 189.
Validity of Two Hour Rat Test for Human Pregnancy. E. J. Farris. —p. 200.
Status of Infant at Birth as Related to Basal Metabolism of Mother in Pregnancy. L. W. Sontag, E. L. Reynolds and Virginia Torbet. —p. 208.
Experimental Basis for Chemotherapy of Trichomonas Vaginalis Infestations: II. R. E. Trussell and G. Johnson.—p. 215.
Salmonella Cholerae Suis Bacteremia During Pregnancy. E. R. Neter, L. A. Siegel and Phyllis Clark.—p. 222.
Control of Menorrhagia by Prolactin. H. S. Kupperman, P. Fried and L. Q. Hair.—p. 228.
Cesarean Section Under Continuous Caudal Analgesia: Supplementary Report. C. B. Lull and J. C. Ullery.—p. 235.
*Acute Pelvic Thrombophlebitis Treated with Continuous Caudal Anesthesia. G. J. Ellis and J. B. Sheffery.—p. 241.
Vaginal Antisepsis: Comparative Study of Bimerphen Solution in 910 Consecutive Deliveries. R. R. Gates.—p. 246.
Vitamin and Endocrine Therapy in Nausea and Vomiting of Pregnancy. B. F. Hart, W. T. McConnell and Alice N. Pickett.—p. 251.
Further Studies on Intrauterine Sulfanilamide Packs. W. E. Brown. —p. 254.
Eclampsia Without Convulsions, Hypertension or Coma. R. A. Reis and E. A. Bernick.—p. 257.
Report of 67 Consecutive Postpartum Sterilizations. B. Diamond. —p. 260.
Brenner Tumor of Ovary Associated with Sarcomatous Change in Fibromyomata Uteri. B. R. Austin and G. W. Ramsey.—p. 263.
Spontaneous Postpartum Disappearance of Massive Condylomata Acuminata of Vulva. W. Footer.—p. 266.

Continuous Caudal Anesthesia in Acute Pelvic Thrombophlebitis.—During the past six months Ellis and Sheffery have used continuous caudal anesthesia in 10 cases of acute pelvic thrombophlebitis with excellent results. Two typical cases are reported. The authors feel that the caudal method has several advantages over the regional sympathetic block of the first, second, third and fourth lumbar sympathetic ganglions. Regional injection requires four punctures, caudal but one. The continuous bathing of the sympathetic chain for several hours is preferable to the one injection technic necessitated by the regional block method. In caudal nerve block it is possible to tell when the needle is correctly placed by the classic signs such as sciatic pain, progressive regional anesthesia, sphincter relaxation and vasodilatation of the extremities. In sympathetic nerve block one cannot be sure that all the ganglions have been correctly injected. In acute thrombophlebitis the authors give 30 cc. (low caudal) every hour until four doses have been given. This intermittent method of injection has the advantage that, if there is a tendency for the vasoconstriction to reestablish itself after the effect of the drug wears off, the impulse can be immediately released again by the next injection.

American Journal of Psychiatry, New York

101:1-140 (July) 1944. **Partial Index**

Current Trends in Military Neuropsychiatry. M. J. Farrell and J. W. Appel.—p. 12.
Psychiatry in the British Army. J. R. Rees.—p. 20.
Psychiatrist Looks at Child Psychiatrist. K. M. Bowman.—p. 23.
Role of X-Rays in Study of Local Atrophic Lesions of Brain. A. E. Childe and W. Penfield.—p. 30.
Observations on Patterns of Anxiety. D. E. Cameron.—p. 36.
Clinical and Electroencephalographic Studies: Correlations of Mental, Electroencephalographic and Anatomic Changes in Cases with Organic Brain Disease. H. Strauss.—p. 42.
Insulin Shock Therapy After Seven Years. E. D. Bond and T. D. Rivers.—p. 62.
Group Psychotherapy: Superior Method of Treating Larger Numbers of Neurotic Patients. S. B. Hadden.—p. 68.
Development of Research Program in Mental Deficiency Over a Fifteen Year Period. R. H. Haskell.—p. 73.
Nature of Psychogenic Cure. C. P. Oberndorf.—p. 91.
Quantitative Use of Rorschach Method: "Instability" and "Disability" Ratings Which Show Clinical and Psychometric Correlations. W. D. Ross.—p. 100.
Startle Neurosis. F. C. Thorne.—p. 105.
Effect of Electric Shock Therapy on Cerebrospinal Fluid Pressure, Protein and Cells. J. S. L. Jacobs.—p. 110.
Review of Psychiatric Progress in Ibero-America. A. C. Pacheco e Silva.—p. 113.

American Journal of Tropical Medicine, Baltimore

24:221-280 (July) 1944

Renewed Clinical Activity in Naturally Induced Vivax Malaria. M. F. Boyd and S. F. Kitchen.—p. 221.
Observations on Possible Usefulness of Complement Fixation Test in Early Diagnosis of Yellow Fever. Alina Perlowagora and E. H. Lennette.—p. 235.
Yellow Fever Control During War. C. L. Williams.—p. 245.
Consideration of Certain Problems Presented by Case of Strongyloidiasis. E. D. Palmer.—p. 249.
Behavior of Trichomonas Vaginalis in Semisolid Medium. M. J. Hogue. —p. 255.
*Vitamin C and Ability to Work in Hot Environments. A. Henschel, H. L. Taylor, J. Brozek, O. Mickelsen and A. Keys.—p. 259.
Medical Care in Belgian Congo. C. A. Flood and W. Sherman.—p. 267.
Apparatus to Facilitate Feeding of Insects on Laboratory Animals. A. Packchanian.—p. 273.

Vitamin C and Ability to Work in Hot Environments.—According to Henschel and his associates claims have been made that large ascorbic acid intakes are of immediate benefit in exposures to high temperature of relatively short duration. The authors report 3 series of studies on 44 normal young men under rigidly controlled conditions of diet, physical work and environment. The ascorbic acid intake was set at two levels: 20 to 40 mg. and 520 to 540 mg. Particular attention was paid to (*a*) cardiovascular functions, (*b*) performance of standard physical tasks, (*c*) psychomotor functions and (*d*) ascorbic acid in sweat, blood plasma and urine. The performance of muscular work was studied in dry heat up to 122 F. The stay in the heat varied from three hours to four days. Comparisons were made between performances on a diet restricted in ascorbic acid intake and a diet supplemented by 500 mg. of ascorbic acid daily. The dietary differences were maintained for periods of four to seven days. Pulse rates in rest and in work, rectal temperatures, vasomotor stability tests, rates of sweating, general observations and subjective reports all failed to demonstrate significant advantage for the men receiving supplements of ascorbic acid. Psychomotor tests and strength tests likewise failed to show any advantage in the ascorbic acid supplementation. There apparently was a slight gain in flicker fusion frequency related to the extra intake of vitamin C. Daily sweat losses were 5 to 8 liters, but the total loss of vitamin C in the sweat is negligible. Heat exhaustion occurred with equal frequency in the vitamin C restricted and supplemented groups.

American Review of Soviet Medicine, New York

1:485-588 (Aug.) 1944

Enzymes and Coenzymes: Review of Biologic Catalysis. J. O. Parnas. —p. 485.
Possible Relationship in Animals Between Tumor Susceptibility and Stability of Tissue Proteins. V. N. Orekhovich.—p. 517.
Cancer of Stomach. A. A. Bocharov.—p. 532.
*New Method of Treating Tetanus. Lina S. Stern.—p. 540.
High Frequency Electric Current in Treatment of Alcoholic Hallucinosis. K. Y. Gruenberg.—p. 544.
War Neuroses in Army and in Civilian Life. T. I. Yudin.—p. 553.

New Method of Treating Tetanus.—Stern points out that the hematoencephalic barrier may prevent certain therapeutic substances from reaching the nerve centers. She proposed to treat tetanus by injecting the antitetanus serum into the cerebrospinal canal through a cisternal puncture. Precautions must be taken to force the solution under predetermined pressure into the ventricles by inserting the needle at a proper angle to prevent the fluid from flowing into the subarachnoid space. Injection of the serum into the subdural or subarachnoid spaces does not produce the desired effect, as the serum then returns to the blood stream without affecting the nerve centers. Animal experiments and veterinary practice demonstrate that when the symptoms of tetanus are manifest serum should be injected not only intramuscularly or intravenously but also into the ventricles by cisternal puncture. She usually injects 15,000 American units by cisternal puncture and from 30,000 to 50,000 American units intravenously or intramuscularly. This course may be repeated if necessary, but it is usually adequate. For the cisternal injection the patient is placed in a modified Trendelenburg position with the head somewhat lower than the body. At the moment of puncture the head is brought forward so that the chin rests on the sternum. The occipital protuberance and the spine of the atlas are palpated as landmarks. The needle is inserted at an acute angle between the two points and

directed inward in the midline. This point places the needle in the first cervical interspace. Resistance is felt at the dura. A relationship has been found to exist between the circumference of the patient's neck and the average depth of puncture. A neck circumference of 40 cm. corresponds to a puncture depth of 49 mm., a neck circumference of 39 cm. to a puncture depth of 47 mm., and so on. After from 10 to 20 cc. of cerebrospinal fluid has been withdrawn, an equal quantity of antitetanus serum warmed to body temperature is introduced. Six cases are described in which this method was used. As a rule, signs of lockjaw began to disappear twenty-four hours after cisternal injection of antitetanus serum. In cases of incipient tetanus a single cisternal injection of the serum was enough to control further development of the process, to effect a general improvement and to mitigate the symptoms of tetanus.

American Review of Tuberculosis, New York

50:85-184 (Aug.) 1944

*Syphilis and Pulmonary Tuberculosis in Negro. R. Hoffman and G. G. Adams.—p. 85.
*Nutrition in Tuberculosis as Evaluated by Blood Analysis. H. R. Getz, Irene S. Westfall and H. J. Henderson.—p. 96.
Epidemiology of Reinoculation Tuberculosis: Epidemiologic Importance of Course of Bacilli and Route of Invasion in Reinoculation Types of Pulmonary Tuberculosis. F. M. Pottenger.—p. 112.
Tuberculous Pneumonia. D. O. Shields.—p. 122.
Recent Advances in Campaign Against Tuberculosis. R. G. Ferguson. —p. 131.
Compulsory Hospitalization of Open Cases of Tuberculosis. A. L. Banyai and A. V. Cadden.—p. 136.
Tuberculosis Rejectee. E. Bunta.—p. 147.
Mediastinal Herniation in Artificial Pneumothorax: Case Report of Bilateral Mediastinal Herniation in Bilateral Pneumothorax and Herniation of Extreme Size and Unusual Type. I. D. Bobrowitz.—p. 150.
Effect of Promin on Experimental Tuberculosis. A. R. Armstrong, M. V. Rae, C. C. Lucas and P. H. Greey.—p. 160.
*Sulfanilamide and Sulfapyridine in Experimental Tuberculosis. C. R. Smith.—p. 163.
Bactericidal Action of Stilbestrol on Tubercle Bacilli. G. H. Faulkner. —p. 167.

Syphilis and Pulmonary Tuberculosis.—Hoffman and Adams report the results of serologic tests for syphilis on 1,705 tuberculous Negroes admitted consecutively to a sanatorium. There were 507 with positive serologic reactions, an incidence of 29.7 per cent of coexisting syphilis and tuberculosis. The bases for comparison were the amount of pulmonary involvement and the predominant type of tuberculous lesion on admission and the percentage of deaths occurring in both groups in relation to the admission classification. There was no significant difference in the amount of pulmonary disease, the predominant type of tuberculous lesion or the percentage of deaths in the negative and positive serologic groups. The difference in the percentage of syphilis between the minimal and the far advanced tuberculosis groups was less than 7 per cent and could not be used to infer that syphilis lowered the resistance to tuberculosis. The presence of syphilis does not alter the course of pulmonary tuberculosis. Before a tuberculous patient is subjected to antisyphilitic treatment his tuberculosis prognosis must be good. The presence of pregnancy and syphilitic contagiousness are the only exceptions. Proof that the use of an arsenical causes tuberculosis to flare up in any 1 case is extremely difficult, if not impossible. The use of fractional doses of arsenicals, because of fear that full doses may activate tuberculosis, is empirical and defeats the purpose of the antisyphilitic treatment. The authors gained the impression that tuberculosis is hardly ever the cause of a false positive reaction.

Nutrition in Tuberculosis as Evaluated by Blood Analysis.—Getz and his associates report the results of a nutritional study of 457 tuberculous and nontuberculous patients attending an outpatient chest clinic. Each assay included a determination of blood hemoglobin, serum proteins, plasma carotene, serum calcium, serum phosphorus and serum phosphatase, as well as plasma ascorbic acid, vitamin A and erythrocyte sedimentation rate. The authors correlate the analyses with the presence or absence and character of tuberculosis and of the individual deficiencies with one another. The subjects were men between 20 and 45. Men with active pulmonary tuberculosis were deficient in ascorbic acid, vitamin A, hemoglobin and serum albumin in the order listed. All nutritional deficiencies were more extensive and profound in tuberculous than in nontuberculous subjects. Subjects with far advanced tuberculosis were especially deficient in ascorbic acid, serum albumin, hemoglobin, vitamin A, carotene and serum calcium in the order listed. Nontuberculous men from the same population group were deficient in ascorbic acid, hemoglobin, vitamin A and serum albumin, but to a lesser degree. Persons with arrested tuberculosis had nutritive levels essentially the same as nontuberculous men. There was more active tuberculosis in the oldest age group (40 to 49) and less of it was in the minimal stage than was found in the younger age groups. Age and hemoglobin showed a negative correlation; the hemoglobin level remained constant as the age advanced. Tuberculous and nontuberculous subjects alike had normal plasma levels of carotene in the presence of abnormally low vitamin A levels, a fact indicating that carotene conversion was inadequate. The plasma ascorbic acid level showed a positive correlation with the erythrocyte sedimentation test when the maximum five minute drop was used, but no correlation was observed when the total sedimentation in one hour was used. The erythrocyte sedimentation rate showed a positive correlation with the serum albumin concentrations. This fact is believed to give the sedimentation test new significance.

Sulfanilamide and Sulfapyridine in Experimental Tuberculosis.—Smith reports observations on four groups of guinea pigs. He found that sulfanilamide causes complete inhibition of tubercle bacillus cultural growth at a dilution of 1:1,000; sulfapyridine causes some inhibition at 1:5,000, complete at 1:1,000. Guinea pigs treated with 340 mg. of drug divided into five daily doses showed blood levels of 10 to 30 mg. per hundred cubic centimeters falling off to lows of 1 to 5 mg. per hundred cubic centimeters during the night. Sulfanilamide levels rose more rapidly than those of sulfapyridine but were less well sustained at night. Following infection with tubercle bacilli, the sulfanilamide and sulfapyridine treated animals were slower in the development of allergy than the controls. There was distinctly less tuberculosis in the sulfanilamide and sulfapyridine treated animals than in the controls and less in the sulfapyridine treated than in the sulfanilamide treated animals. These differences were shown by fewer and smaller tubercles in the visceral organs, by less caseation in viscera and internal lymph nodes and by smaller spleens and smaller internal lymph nodes. The average arbitrary units of disease per animal were 9.6 for the controls, 6.5 for the sulfanilamide treated and 4.2 for the sulfapyridine treated group. The local lesions, on the other hand, including sites of inoculation and inguinal lymph nodes, were as large in the treated as in the control groups or larger.

Annals of Internal Medicine, Lancaster, Pa.

21:173-366 (Aug.) 1944

*Glycosuria in Meningitis. F. Ferguson and D. Barr.—p. 173.
Waterhouse-Friderichsen Syndrome: Observations on Associated Adrenal Insufficiency and Report of 4 Cases. S. W. Cosgriff.—p. 187.
*Meningococcic Meningitis: Sulfadiazine Therapy (Review of 20 Cases). E. H. Grieco and A. M. Cove.—p. 194.
Meningococcemia Without Meningitis: Study Made at Station Hospital, Fort George G. Meade, Maryland. H. W. Potter, R. D. Reid and L. H. Bronstein.—p. 200.
Medical Problems in Middle East. C. F. Sams.—p. 215.
*Heterophile Antibody Reaction in Infectious Mononucleosis. R. E. Kaufman.—p. 230.
"Atypical" Coronary Disease in Young People. J. Weinstein.—p. 252.
Syphilis and Diabetes Mellitus: Long Term Clinical Study. F. S. Perkin.—p. 272.
Cirrhosis of Liver: Analysis of 71 Cases. I. D. Fagin and F. M. Thompson.—p. 285.
Some Notes on Transmission of Heart Murmurs. S. A. Levine and W. B. Likoff.—p. 298.

Glycosuria in Meningitis.—Ferguson and Barr reviewed records of 72 patients with meningitis admitted to New York Hospital, 30 of whom showed glycosuria. Fourteen of the 30 had received infusions of dextrose solution at some time before the appearance of glycosuria. In the remaining 16 patients cause for the glycosuria other than the meningitis itself was not evident. Glycosuria was encountered in meningitis caused by the meningococcus, the pneumococcus, the staphylococcus, the tubercle bacillus and in 1 case in which the causative organism was not isolated. Glycosuria was accompanied in many instances by ketosis, hyperglycemia and diminished tolerance to sugar. Glycosuria was transient, disappeared in all cases and persisted beyond the third day in only 3 of the 16 cases. Coma with glycosuria and ketosis at the onset of meningitis may mask

the signs of meningeal involvement, lead to a diagnosis of diabetic acidosis and cause serious or fatal delay in instituting appropriate treatment for the meningitis.

Sulfadiazine in Meningococcic Meningitis.—Grieco and Cove review the clinical features of 20 consecutive cases of meningococcic meningitis observed in the course of a year at the Station Hospital, Fort Totten, New York. The cases were sporadic. Sulfadiazine and its soluble sodium salt was the only sulfonamide utilized. Polyvalent antimeningococcus serum was administered intravenously in 1 of the earliest cases in conjunction with chemotherapy. Such a severe reaction ensued that thereafter the use of serum was abandoned. As soon as the diagnosis was verified, an initial dose of 5 Gm. of sodium sulfadiazine in 100 cc. of distilled water was administered intravenously. Subsequent doses of 2 Gm. were then given regularly every four hours for the next twenty-four hours, either orally or intravenously, as determined by the patient's ability to ingest or retain the medication. Then 1 Gm. doses were given every four hours until the temperature returned to normal, and from this point on four times daily for the next seven days. With this medication, adequate blood concentrations were attained and satisfactory clinical responses resulted. The Waterhouse-Friderichsen syndrome was diagnosed clinically in 1 case. The use of adrenal cortex extract was a life saving measure in this instance. This survival on substitutional therapy augurs well for this much dreaded complication. Two deaths resulted in this series of 20 cases. One occurred within less than twelve hours after the onset of the disease, the other four days after admission. Necropsy in the latter revealed a severe bilateral hemorrhagic necrosis of the adrenals.

Heterophile Antibody Reaction in Infectious Mononucleosis.—The present concept is that there are three types of sheep cell agglutinins: those in normal serum absorbed by guinea pig kidney but not by beef erythrocytes, those in the serum of patients with infectious mononucleosis absorbed by beef erythrocytes but not by guinea pig kidney and those in the serum of persons treated with horse serum absorbed by both guinea pig kidney and beef erythrocytes. In this country the Paul Bunnell and Davidsohn methods are standard procedures. Kaufman describes changes made in the Davidsohn technic, the net result of which is that the test is simplified, is just as accurate and gives considerably quicker results. Telephoned reports can be given within one hour of the time of arrival of the serum in the laboratory, if speed of diagnosis is important, which it occasionally is in a questionable case of infectious mononucleosis thought to be acute appendicitis, meningitis, typhoid, mumps or diphtheria. So much time is saved by these modifications in technic that many more specimens can be examined in a day. During a three year period 83 proved cases of infectious mononucleosis have been investigated. In the diagnosis of this disease there are three aspects to consider: the clinical, the hematologic and the serologic. It is felt that if any two of them are definite the diagnosis may be considered established. Tests were performed in 78 of 83 cases of infectious mononucleosis. It is believed that agglutination in a dilution of 1:28 with the "correct" differential absorption tests is a positive reaction. A positive test supports the diagnosis of infectious mononucleosis, but a negative test does not rule it out. The reaction may become positive as early as the third day but sometimes not until the second month or not at all. The reaction usually remains positive for two to four months.

Archives of Physical Therapy, Chicago

25:455-506 (Aug.) 1944

Future Development of Physical Medicine. G. M. Piersol.—p. 455.
*Treatment of Bronchial Asthma by Intensive Breathing Therapy. H. I. Weiser.—p. 461.
Rehabilitation of Convalescent Industrial Ca..ualties with Physical Medicine. H. D. Storms.—p. 469.
Fluorescence Test for Real and Apparent Death in Warfare. J. De Ment.—p. 472.
Army Rehabilitation Program for Blind and Deafened. C. C. Hillman.—p. 478.
Trench Foot. R. C. Berson and R. J. Angelucci.—p. 482.

Breathing Therapy in Bronchial Asthma.—Weiser treated asthmatic patients who had failed to respond to other treatments by breathing therapy. His intensified breathing therapy consists of massage, rhythmic compressions of the thorax and breathing exercises. Intensive gymnastics are of special importance. These include sports (boxing, jujutsu, calisthenics) associated with regulated breathing. The exercises must be performed daily over a period of months or even years. Dyspnea is produced by physical strain during each treatment, but with the aid of the acquired technic of respiration it is soon "breathed away." The patient learns how to master dyspnea by concentration and regulation of respiration. Courage training, boxing, apparatus gymnastics and increased efforts during the course of treatments increase self confidence in the asthmatic patient. Intensified breathing therapy should be supervised by the physician. The vital capacity, expiration time and breathing span were always considerably increased during the course of treatments. The absolute value for vital capacity cannot be taken as a criterion for a prognosis. Prognostic conclusions can be drawn from curves derived from the vital capacity and expiration time measured during each treatment. In the study reported, the minimum time of observation after treatment was twelve months. It was possible to keep 13 among 39 juvenile asthmatic patients free from attacks; they were under observation for three and one-half years. The disease in 10 of these 13 had lasted for more than two years before the treatment was instituted. Ten of the 29 children continued to show improvement. Six remained uninfluenced. Of 10 asthmatic adults, 1 was freed of attacks, 5 improved and 4 were not affected.

Archives of Surgery, Chicago

49:1-74 (July) 1944

*Early Ambulation Following Section of Anterior Abdominal Wall: Analysis of 426 Personally Conducted Cases. H. Nelson.—p. 1.
Cystic Tumor of Iliopectineal Bursa: Report of 2 Cases. V. R. Stephens.—p. 9.
Clinical Observations on Tissue Temperatures: Pathologic and Therapeutic Effects. F. K. Safford Jr. and M. B. Nathanson.—p. 12.
Effect of Experimental Fracture on Bone, Dentin and Enamel: Study of Mandible and Incisor in Rat. B. G. Sarnat and I. Schour.—p. 23.
*Peritoneal Tap. L. R. Kaufman, W. P. Eckes and J. Mule.—p. 39.
Alkaline and Acid Phosphatase Levels in Serum of Dogs After Ligation of Common Bile Duct. J. L. Carr and F. S. Foote.—p. 44.
Local Implantation of Gelatin in Wounds. J. A. Sinclair and B. Douglas.—p. 47.
*Cavernous Hemangioma of Lung (Arteriovenous Fistula): Report of Case with Successful Treatment by Pneumonectomy. W. E. Adams, T. F. Thornton Jr. and Lillian Eichelberger.—p. 51.
Review of Urologic Surgery. A. J. Scholl, F. Hinman, A. von Lichtenberg, A. B. Hepler, R. Gutierrez, G. J. Thompson, E. N. Cook, E. Wildbolz and V. J. O'Conor.—p. 59.

Early Ambulation Following Abdominal Section.—Nelson reports observations on 426 personally conducted cases. As soon as the patient has fully recovered from the effects of anesthesia, the bed is sharply tilted, so that the head is elevated. After this position has been maintained for a time the bed is leveled and the patient assumes a sitting position on the side of the bed, with the feet resting on a chair. In this position he breathes deeply and coughs frequently. He then lies down, and the head of the bed is again sharply elevated. After a second period of rest he is assisted to stand and is conducted to the bathroom, where the bladder is practically always emptied without difficulty. If his condition is good he sits up in a chair for a time before returning to bed. Those who are oversensitive to the pain of the first rising or who are unduly apprehensive are made to practice sitting at the edge of the bed, with intervals of rest after each attempt, until they are strong enough and willing to walk to the bathroom. The majority of patients walked on the day of operation or within the first twenty-four hours. The incidence of immediate and delayed complications in this series was minimal. Of the three partial disruptions of a wound two occurred in patients whose wounds had been closed with catgut and for whom early ambulation had not been authorized. Only two incisional hernias were observed. The single fatality in the series was due to cerebral thrombosis. Good results depend on the strict observance of contraindications as well as of indications. Contraindications to early ambulation are: 1. Failure to observe the prerequisites of optimum healing of wound, including failure to carry out the tenets of Halsted as to the closure of a wound, the use of suture materials other than wire or cotton and the existence of deficiencies of vitamins and hypoproteinemia. 2. Conditions such as shock, peritonitis, active hemorrhage, cardiac failure, pneumonitis and impending

or actual thyroid crisis. 3. Potential or actual complications including gross contamination, infection, hemorrhage and dehiscence. 4. Pregnancy in which abortion is feared. 5. Extreme debility, for which ambulation is deferred until there is some restoration of strength and muscle tone, as a result of sitting up. 6. Second stage of a thoracolumbar sympathectomy, after which the patient, because of sudden alterations in the vascular system, cannot immediately tolerate the upright position. 7. Lack of adequate and intelligent nursing supervision. The advantages of early ambulation include the lowered incidence of postoperative complications, particularly pulmonary and vascular complications; the lower incidence of nausea, vomiting and abdominal distention; the earlier return of normal function of the bladder and the bowel; the maintenance of normal muscle tone; the psychologic effect on the patient's morale and mental status; the acceleration of convalescence and the earlier return of working ability, and the economic savings to the patient and the hospital.

Peritoneal Tap.—Kaufman and his associates say that their interest in peritoneal tap was stimulated when they began an exhaustive study of perforation of peptic ulcers in an effort to reach an early diagnosis by administering methylene blue by mouth and recovering the dye by peritoneal puncture. Peritoneal tap is performed with a number 18 or 19 gage needle 2½ inches long through a small procaine hydrochloride wheal in the midline below the navel or to either side or in the epigastrium. Peritoneal tap is a practical and safe procedure which requires extreme care in removal of the peritoneal contents and study of the smears and which affords evidence of the peritoneal reaction present by a simple and rapid laboratory study. In children the procedure serves to differentiate streptococcic and pneumococcic peritonitis from appendicitis. While a positive result of a tap is of diagnostic value, a negative result should be disregarded, especially in the face of other diagnostic signs; a negative result indicates usually only failure to obtain fluid which is present. Peritoneal tap should be reserved for selected cases presenting confusion in diagnosis, and the interpretation of the smear must be painstaking. In cases in which perforated peptic ulcer is suspected, when diagnostic data are confusing and likely to lead to exploratory laparotomy, the recovery by peritoneal tap of methylene blue previously introduced into the stomach will establish the exact diagnosis. While the results of the procedure were of definite clinical value in only 14 of their 22 cases, the diagnosis in all of these presented great difficulties and could be established accurately only by exploratory laparotomy. The tap in these cases established data that determined diagnosis and aided definitely in treatment as well as in evaluation of prognosis.

Cavernous Hemangiona of Lung.—Adams and his associates stress the rarity of hemangioma of the lung, pointing out that the case reported by them was the first in more than 240,000 admissions at the University of Chicago Clinics in the last fifteen years, and more than 4,380 necropsies at the same institution did not reveal another such lesion. A man aged 24 entered the University Clinics complaining of frequent nosebleeds and colds over the last two or three years. He also had suffered from generalized cyanosis and clubbing of the fingers and toes for at least sixteen years. A roentgenogram of the chest revealed a large, irregularly shaped, circumscribed opacity in the left lung and a small one in the right lung. There were associated compensatory polyemia, polycythemia and hyperhemoglobinemia. After removal of the left lung the status of the blood approached the normal and the patient returned to work. Most investigators who have reported cases similar to the 1 presented here have described the lesion as a cavernous hemangioma. A careful study of the microscopic sections made from the specimen removed from their patient revealed only normal pulmonary tissue surrounding the three separate mesothelium lined cavities found in the left lung. On the basis of the pathologic picture the lesions are really arteriovenous aneurysms or fistulas. The pulmonary lesion produced a great compensatory change in the quality and the quantity of the blood. Polycythemia (7,200,000 cells) was present before operation with a corresponding increase in red cell mass (hematocrit reading 82 per cent) and hemoglobin (23 Gm. per hundred cubic centimeters). The blood volume was approximately two times the normal amount, the increase being entirely in the red cell mass. After the removal of the left lung, all of the blood was diverted to the right side and was aerated as it passed through the right lung. The red cell count fell more than 2,000,000 within two days and has remained at a high normal level. The hemoglobin content was reduced from a preoperative level of 23.0 Gm. to the present level of 15.7 Gm. per hundred cubic centimeters. The hematocrit reading was likewise reduced from 82 to 54 per cent. The estimated total blood volume fell from 12,750 cc. (preoperative) to 6,900 cc. by the second postoperative day, this reduction being entirely in the erythrocytes. Ten days later the blood volume was 6,350 cc., a value which is approximately normal. Although only 4 similar cases have been previously reported, the condition in others has probably gone undiagnosed and been treated as polycythemia vera. When clubbing of the fingers and the toes is present, some pulmonary lesion should be suspected and a roentgen examination of the lungs made. A correct diagnosis may be readily established on the basis of altered values of blood oxygen and the finding of an opacity in the lung on roentgen examination.

Bulletin of Johns Hopkins Hospital, Baltimore

74:321-426 (June) 1944

Effect of Testosterone Propionate on Arterial Blood Pressure, Kidneys, Urinary Bladder and Livers of Growing Dogs. S. S. Blackman Jr., Caroline Bedell Thomas and J. E. Howard.—p. 321.
Experimental Hypertension from Section of Moderator Nerves: Relationship of Acute Pressor Response to Development and Course of Chronic Hypertension. Caroline Bedell Thomas.—p. 335.
*On Isolation and Properties of Fluorescent Factor F_2 from Human Urine. V. A. Najjar, Virginia White and D. B. McScott.—p. 378.
Laboratory Diagnosis of Nicotinic Acid Deficiency: An Improved Procedure for Determination of F_2 (N-Methyl Nicotinamide Derivative) in Urine. V. A. Najjar.—p. 392.
*Case of Pellagra Developing on Hospital Ward in Patient Receiving Vitamin B Complex. D. W. Roberts and V. A. Najjar.—p. 400.
Anti-Blacktongue Activity of N-Methyl-Nicotinamide Chloride. V. A. Najjar, Margaret M. Hammond, Mary Allen English, Maria B. Wooden and Carolyn C. Deal.—p. 406.

Fluorescent Factor F_2 in Human Urine.—Najjar and Wood described in 1940 the presence in urine of a substance with a characteristic bluish fluorescence the excretion of which was related to the availability of nicotinic acid, being increased in proportion to the nicotinic acid intake. This substance, designated as F_2, was regularly absent from the urine of patients with pellagra. In this paper Najjar and his associates show that the highly fluorescent compound F_2 obtained on treating urinary eluates with alkali and butanol is apparently derived from a precursor which shows only a slight bluish fluorescence. The procedure used—alkalization and butanol extraction—serves to convert this precursor into the highly fluorescent compound F_2. The identity of the urinary precursor is not yet completely established. The highly fluorescent substance F_2, formed from the urinary precursor, appears to be a butyl ether of N-methyl nicotinamide alphacarbinol.

Pellagra Developing in Hospital Patients Receiving Vitamin B Complex.—Roberts and Najjar report the history of a girl aged 12. Between August 1942 and April 1943 the patient's weight decreased from 78 pounds (35 Kg.) to 60 pounds (27 Kg.). The most conspicuous symptom during this period was anorexia. Although offered a liberal diet containing cereal, eggs, bacon, green vegetables, meat, potatoes and a quart of milk daily, only small amounts of the quantity offered were taken. The patient was frequently nauseated and at times vomited after meals. Following admission to the hospital in April 1943 the patient continued a downward course. Therapy consisted in a high caloric diet supplemented with orange juice and a liquid extract of yeast, given in doses of 4 cc. per day, to furnish the B complex. The hemoglobin fell to 8 Gm. but responded well to a transfusion. In spite of the supportive measures the patient continued to lose weight gradually. Eight weeks after admission it was noticed that a symmetrical brown pigmentation had developed on the backs of the hands, extending up to the knuckles, where it was sharply demarcated from the pale skin beyond. Brown pigmented areas were likewise noted over the calluses of the elbows. The suspicion of pellagra was borne out by the tongue, which was red, notably at the margins, and showed atrophy of the papillae. The diagnosis was confirmed by studies of the excretion of the fluorescent

factor F_2 (N-methyl nicotinamide derivative) in the urine. Some light on the pathogenesis of the pellagra was obtained from a consideration of the vitamin content of the yeast extract which had been used in treating the patient. It was found that the daily dose which the patient had been getting contained 0.3 mg. of thiamine and 10 mg. of riboflavin but only insignificant amounts of nicotinic acid. The authors suggest that an obscure intestinal disorder, perhaps of the nature of a regional ileitis, interfered with intestinal absorption to an extent sufficient to cause pellagra. It is pointed out that certain commercial yeast extracts do not supply sufficient quantities of nicotinic acid.

Bulletin New York Academy of Medicine, New York

20:427-470 (Aug.) 1944

*Jaundice Following Administration of Human Serum: Harvey Lecture, March 16, 1944. J. W. Oliphant.—p. 429.
Major Therapeutic Trends in American Psychiatry. J. C. Whitehorn.—p. 446.
Shoulder Pain and Disability. D. M. Bosworth.—p. 460.

Jaundice Following Administration of Human Serum.—Oliphant shows that jaundice following administration of materials containing serum of the homologous species has been observed repeatedly both in man and in the lower animals. It is still unknown whether this type of jaundice is identical with naturally occurring so-called infectious hepatitis. The author presents the results of a sample survey of an epidemic of jaundice occurring subsequent to vaccination against yellow fever in the Virgin Islands in 1942. Jaundice was produced experimentally (1) by the inoculation of two lots of yellow fever vaccine containing human serum, (2) by the inoculation of small amounts of filtered serum from each of 3 persons and of a serum pool from 9 persons all of whom had previously received yellow fever vaccine containing human serum and (3) by inoculation of serum from 1 person who had early spontaneously occurring jaundice. Two serums which were icterogenic when inoculated subcutaneously failed to produce jaundice by the intranasal route. Persons of all four Moss blood groups and both Rh positive and Rh negative persons were found to be susceptible. Susceptible persons did not give uniform local skin reactions to icterogenic serums. The jaundice producing agent is filtrable and survives drying in vacuum, storage for long periods in serum at 4 C. and heating to 56 C. for one-half hour in the dried state. The agent was found to be present in the blood during the prejaundice period but not two and one-half months after the disappearance of jaundice. The icterogenic agent is apparently inactivated by short exposure to ultraviolet irradiation. Transmission of jaundice by ordinary contact apparently did not occur during this experiment. Attempts to produce jaundice in experimental animals were unsuccessful. Antigens prepared from human livers and from chick embryos failed to fix complement in the presence of serums obtained after recovery from jaundice.

Bull. of the U. S. Army Med. Dept., Washington, D. C.

79:1-122 (Aug.) 1944

Anesthesia in Combat Zone. G. Shortz.—p. 60.
Cutaneous Leishmaniasis. D. Ball and R. C. Ryan.—p. 65.
Oral Rehabilitation: Case Report. R. C. Reichert.—p. 74.
Herniated Nucleus Pulposus: Improvement in the Operative Technic. R. C. L. Robertson and W. G. Peacher.—p. 76.
Surgical Problems in Buna Campaign. A. Thorndike.—p. 77.
Vaccinia Occurring at Short Intervals. C. A. Minning.—p. 82.
Inspection of Fish of Pacific Northwest. E. W. Bloomquist.—p. 84.
Diagnosis of Dengue. G. V. LeRoy and H. A. Lindberg.—p. 92.
*Experimental Use of Penicillin in Treatment of Sulfonamide Resistant Gonorrhea. R. J. Murphy.—p. 101.
Modified Orthopedic Table Constructed in Field. V. Mayer.—p. 105.
Psychoses in Army: Follow-Up Study. N. Q. Brill and E. F. Walker.—p. 108.

Penicillin in Sulfonamide Resistant Gonorrhea.—Murphy treated 306 cases of sulfonamide resistant gonorrhea with penicillin. Of this number 262 cases were cured following the first trial on penicillin. Thirty-four failures following the first treatment were treated again according to another schedule, with recovery in all but 3. These 3 were treated again and now responded. The treatment consisted of a total of 100,000 units given over a twelve hour period in five doses of 20,000 units. The foremost clinical observation was the persistence of urethritis following treatment. The character of the discharge changed from a purulent to a thin watery one. The mucous membrane of the urethra remained inflamed, glistening and moist beyond the time of disappearance of the watery discharge. In the majority of cases it was about one week after treatment before all evidence of the infection disappeared. In spite of the persistence of discharge and inflammation, all subjective symptoms such as dysuria, polyuria, hematuria and nocturia usually had subsided by the time the last treatment had been administered. The urine, after becoming clear, retained shreds in the majority of cases throughout the entire follow-up period. Only 1 patient had a generalized urticaria five days following treatment, which persisted for three days. Gonorrheal conjunctivitis is cured by the intramuscular administration of penicillin. Acute suppurative prostatitis responds slowly but favorably. Four cases of gonorrheal arthritis with concomitant gonorrheal urethritis showed no benefit from penicillin and in every case following the cure of the urethritis other treatments for the arthritis were required.

Canadian Medical Association Journal, Montreal

51:99-194 (Aug.) 1944

Social Implications of Scientific Research. J. R. Williams.—p. 99.
*Further Studies on Relationship of Corneal Vascularization to Riboflavin Deficiency. J. F. McCreary, J. V. V. Nicholls and F. F. Tisdall.—p. 106.
*Closed Plaster Method in Prevention of Shock After Burns. E. A. Sellers and E. S. Goranson.—p. 111.
Wartime Pressures. D. E. Cameron.—p. 114.
Epidemic Jaundice. A. Somerville and J. S. Clark.—p. 120.
Problem of Nasal Medication, with Particular Reference to Privine HCl 0.1 per Cent. J. Gollom.—p. 123.
Vertigo. J. P. Boley.—p. 126.
Condyloma Acuminata or Genital Warts in Female (Report of Case). H. Dover.—p. 132.
Medical Education: Interns and Residents. J. C. Mackenzie.—p. 134.
Typhoid Epidemic in Southern Alberta. F. W. Gershaw.—p. 138.
Tuberculosis Concepts Then and Now. D. F. McRae.—p. 139.
First Aid and Transportation in Cases of Fracture or Suspected Fracture of Spine. G. P. Howlett.—p. 142.
Procedures Recommended for Organization and Operation of Blood Bank: Part II. Procedures. L. J. Rhea, O. F. Denstedt, A. Bertrand, G. J. E. van Dorsser and P. H. Greey.—p. 144.

Corneal Vascularization and Riboflavin.—McCreary and his associates report studies to determine whether or not a slit lamp examination and the photographic procedure give comparable data and to throw further light on the effect of riboflavin on corneal vascularization and symptoms of eye fatigue. The results obtained from photographing the corneoscleral junction with the ophthalmic camera and by an examination with a slit lamp are not significantly different. A study to demonstrate the effect of riboflavin on corneal vascularization has been carried out, using both photography and the slit lamp examination. The subjects studied were 41 students in the photographic division of the Canadian Air Force who had been provided with a ration containing when served 2.9 mg. of riboflavin per day for a period of one year. Approximately one half of the subjects were given a supplement of 3.3 mg. of riboflavin three times a day for two months and the others received placebos. There was no consistent change in corneal vascularization in either the treated subjects or the controls. The instillation of a simple irritant in the conjunctival sac caused collapsed, afunctional blood vessels in the cornea, transitional zone and conjunctiva to become engorged. As far as this study shows, it seems that a uniform peripheral corneal vascularization is not a safe basis for a diagnosis of riboflavin deficiency existing at the time of examination. Such a lesion may be due to riboflavin deficiency, but the deficiency could have occurred at any time previous to the examination. Also these blood vessels could have been reactivated by some cause other than lack of riboflavin.

Closed Plaster Method in Prevention of Shock.—According to Sellers and Goranson mortality from shock was greatly reduced when plastering was carried out immediately after the burn. They report a series of experiments designed to show whether any benefit in this respect can be derived from later application of plaster or from "pressure" dressings. It was found that immediate application of plaster bandages

decreases the mortality rate and hemoconcentration to a great degree. Some benefit in this respect accrues from application within one hour. Immediate application of plaster is more effective in decreasing the mortality rate from shock than is the immediate application of pressure dressings. As these experiments were performed with animals and under laboratory conditions, conclusions drawn from them should be accepted with reservations as to direct clinical application.

Georgia Medical Association Journal, Atlanta

33:201-236 (July) 1944

Hypertension: Examination of Patients. H. M. Davison, H. Bowcock and E. Vogt.—p. 201.
Medical Conservation of Manpower in Shipyard. R. L. Brown.—p. 208.
Georgia's Postwar Public Health Program. T. F. Abercrombie.—p. 213.

33:237-264 (Aug.) 1944

Ulcers of Stomach and Duodenum. A. W. Allen.—p. 237.
Penicillin in Acute and Chronic Infections. A. L. Evans.—p. 249.
Psychoanalysis: Christ versus Freud. E. S. Osborne.—p. 251.

Journal of Clin. Endocrinology, Springfield, Ill.

4:229-286 (June) 1944

*Thiouracil Treatment in Hyperthyroidism. E. B. Astwood.—p. 229.
*Treatment of 26 Thyrotoxic Patients with Thiouracil and Review of Toxic Reactions in All (135) Reported Cases. T. H. McGavack, A. J. Gerl, Mildred Vogel and D. Schwimmer.—p. 249.
Human Pregnancy Test Based on Color Reaction of Pregnandiol in Urine. H. S. Guterman.—p. 262.
Protein Bound Plasma Iodine in Patients with Thyroid Disease: I. Correlation with Basal Heat Production. B. E. Lowenstein, M. Bruger and J. W. Hinton, with technical assistance of S. Member.—p. 268.
Case of Probable Pan-Hypopituitarism Following Postpartum Pituitary Necrosis. S. J. Glass.—p. 273.

Thiouracil Treatment in Hyperthyroidism.—Astwood reviews observations on 62 persons who have been given repeated doses of thiouracil. Eleven had normal thyroids, while 51 had hyperthyroidism. Large nodular goiters were not common. Forty-one of the 51 cases were considered to be diffuse hyperplastic goiter with hyperthyroidism. In 8 of these iodine had been given shortly before thiouracil. The administration of 0.2 to 0.6 Gm. of thiouracil daily in two doses quickly controlled all the manifestations of hyperthyroidism in previously untreated cases. The metabolic response was slower in most cases of toxic nodular goiter, in iodine treated diffuse hyperplastic goiter with hyperthyroidism and in normal persons. A temporary enlargement and increased vascularity of the thyroid gland was noted in some cases. Exophthalmos usually improved slowly. Iodine still exhibited its characteristic effect on patients both during and after thiouracil therapy. Serious side-effects consisting of granulocytopenia and drug fever occurred in about 10 per cent of the cases during the early weeks of therapy. Adequate treatment, continued for longer than six months, was attended by a high incidence of lasting remissions.

Thiouracil in Thyrotoxic Patients.—McGavack and his associates observed 4 male and 22 female patients while under treatment with thiouracil. Fourteen of the patients were hospitalized, while the other 12 made no change in their usual routine of living. The patients were followed for periods ranging from six days to nine months. Characteristic effects in the adequately treated patient included a lowering of the basal metabolic rate, a decrease in pulse rate, a narrowing of the pulse pressure with diminution in the systolic figure, an increase in weight and an elevation of the value for total blood cholesterol. The size of the thyroid was moderately decreased under treatment with thiouracil, and creatinuria was diminished. No variations in blood chlorides, sodium or potassium were observed. Tests of liver function failed to show abnormality before or during treatment. A table lists the incidence of toxic reactions in 109 cases in which thiouracil had been given which had been previously reported by others and in the 26 here presented. In the total of 135 cases studied to date there were 16 (11.5 per cent) that exhibited a toxic or hypersensitivity reaction. Two of the 26 patients had severe toxic reactions. One developed agranulocytosis, the other a fever and widespread urticarial rash. The authors think that results of therapy with thiouracil have been sufficiently promising to warrant its extended and prolonged use in cases of toxic hyperplasia with a view to avoiding operative procedure. However, in this connection the toxic action must ever be kept in mind, and the clinician must be prepared to change his course when faced with early signs of unfavorable reaction.

Journal of Clinical Investigation, Boston

23:417-606 (July) 1944. **Partial Index**

Chemical, Clinical and Immunologic Studies on Products of Human Plasma Fractionation: I. Characterization of Protein Fractions of Human Plasma. E. J. Cohn, J. L. Oncley, L. E. Strong, W. L. Hughes Jr. and S. H. Armstrong Jr.—p. 417.
Id.: II. Electrophoretic and Ultracentrifugal Studies of Solutions of Human Serum Albumin and Immune Serum Globulins. J. W. Williams, Mary L. Petermann, G. C. Colovos, Martha B. Goodloe, J. L. Oncley and S. H. Armstrong Jr.—p. 433.
Id.: III. Amino Acid Composition of Plasma Proteins. E. Brand, Beatrice Kassell and L. J. Saidel.—p. 437.
Id.: IV. Study of Thermal Stability of Human Serum Albumin. G. Scatchard, S. T. Gibson, L. M. Woodruff, A. C. Batchelder and A. Brown.—p. 445.
Id.: V. Influence of Nonpolar Anions on Thermal Stability of Serum Albumin. G. A. Ballou, P. D. Boyer, J. M. Luck and F. G. Lum.—p. 454.
Id.: VII. Concentrated Human Serum Albumin. C. A. Janeway, S. T. Gibson, L. M. Woodruff, J. T. Heyl, O. T. Bailey and L. R. Newhouser.—p. 465.
Id.: VIII. Clinical Use of Concentrated Human Serum Albumin in Shock and Comparison with Whole Blood and with Rapid Saline Infusion. A. Cournand, R. P. Noble, E. S. Breed, H. D. Lauson, E. deF. Baldwin, G. B. Pinchot and D. W. Richards Jr.—p. 491.
Id.: IX. Treatment of Shock with Concentrated Human Serum Albumin; Preliminary Report. J. V. Warren, E. A. Stead Jr., A. J. Merrill and E. S. Brannon.—p. 506.
Id.: X. Concentrations of Certain Antibodies in Globulin Fractions Derived from Human Blood Plasma. J. F. Enders.—p. 510.
Id.: XI. Use of Concentrated Normal Human Serum Gamma Globulin (Human Immune Serum Globulin) in Prophylaxis and Treatment of Measles. J. Stokes Jr., E. P. Maris and S. S. Gellis.—p. 531.
Id.: XIV. Appraisal of Isohemagglutinin Activity. E. L. DeGowin.—p. 554.
Id.: XVI. Fibrin Clots, Fibrin Films and Fibrinogen Plastics. J. D. Ferry and P. R. Morrison.—p. 566.
*Id.: XVIII. Fibrinogen Coagulum as Aid in Operative Removal of Renal Calculi. J. E. Dees.—p. 576.
*Id.: XIX. Note on Use of Fibrinogen and Thrombin in Surface Treatment of Burns. C. v. Z. Hawn, E. A. Bering Jr., O. T. Bailey and S. H. Armstrong Jr.—p. 580.
Id.: XX. Development of Fibrin Foam as Hemostatic Agent and for Use in Conjunction with Human Thrombin. E. A. Bering Jr.—p. 586.
Id.: XXII. Fibrin Films in Neurosurgery, with Special Reference to Their Use in Repair of Dural Defects and in Prevention of Meningocerebral Adhesions. O. T. Bailey and F. D. Ingraham.—p. 597.
Id.: XXIII. Effects of Feeding Possible Blood Substitutes on Serum Protein Regeneration and Weight Recovery in Hypoproteinemic Rat. P. R. Cannon, Eleanor M. Humphreys, R. W. Wissler and L. E. Frazier.—p. 601.

Fibrinogen Coagulum in Removal of Renal Calculi.—Dees describes a new aid in the removal of small free stones from the renal pelvis at open operation. By the simultaneous injection of solutions of fibrinogen and thrombin, a strong coagulum which completely fills the pelvis and enmeshes all free stones is produced. On withdrawing this coagulum through the usual pyelotomy incision, all free stones should be removed. Fragmentation of calculi and trauma to the kidney are thus avoided. This operative procedure has been carried out on 21 patients without demonstrable ill effect.

Fibrinogen and Thrombin in Surface Treatment of Burns.—Hawn and his associates point out that, when large quantities of purified human fibrinogen and thrombin became available through the fractionation of human plasma to prepare albumin for the armed forces, studies were undertaken to develop from these proteins, which constitute important components in the natural mechanism for the protection of wounds, a dressing which would meet the specifications for an agent for the surface therapy of burns. They present observations on surgically denuded areas of animals and burns on human beings which suggest that human fibrinogen and thrombin mixtures have no deleterious effect on normal processes of repair. The use of preformed fibrin films prepared from the proteins involved in the natural coagulation mechanism is described in a small series of second and third degree burns. Such films are susceptible of adaptation to many programs of surface therapy. It is suggested that such films, particularly in the form of roll bandages, might prove a highly expedient fibrinogen-thrombin dressing for burns in the field, owing to simplicity and speed from the standpoint of application and to lack of bulk from the standpoint of transportation.

Journal of Lab. and Clinical Medicine, St. Louis

29:785-888 (Aug.) 1944

*Clinical Use of Phthalylsulfathiazole. E. J. Poth and C. A. Ross.—p. 785.
Acute Toxicity of Commercial Penicillin. H. Welch, C. W. Price, J. K. Nielsen and A. C. Hunter.—p. 809.
Actinomycosis: Report of Case with Miliary Chest Lesions. A. M. Harris and J. B. Priestley.—p. 815.
Local Eosinophilia in Malignant Neoplasms. A. J. Gill.—p. 820.
Subacute Bacterial Endocarditis Confined to Pulmonic Valve with Malformed Leaflets. R. J. Rogers.—p. 825.
Note on Possible Allergic Factor in Altitude Sickness. Julia Baker.—p. 831.
Effect of Heparin on Phagocytosis: Observations on P. Lophurae in Chick. R. H. Rigdon.—p. 840.
Effect of Gonads and Adrenals on Absorption of Subcutaneous Sesame Oil. C. E. Tobin.—p. 850.
Effect of Bile Acids on Biliary Excretion of Neoarsphenamine and Mapharsen. J. H. Annegers, F. E. Snapp, A. C. Ivy and A. J. Atkinson.—p. 853.

Clinical Use of Phthalylsulfathiazole.—Poth and Ross say that an extensive study covering twenty acylated sulfonamides in an attempt to find substances possessing antibacterial properties and being poorly absorbed from the alimentary tract has resulted in the synthesis and discovery of several compounds fulfilling these specifications. They report experiences with phthalylsulfathiazole, a condensation product of sulfathiazole and phthalic anhydride. It is an antibacterial agent of considerable interest and of therapeutic possibilities when activity restricted to the alimentary tract is desired. Approximately 5 per cent of the orally administered therapeutic dose is excreted in the urine. Ordinarily the concentration of the drug in the blood does not exceed 1.5 mg. per hundred cubic centimeters. As compared to their respective bacteriostatic activities, when measured by their ability to suppress the coliform organisms, phthalylsulfathiazole possesses roughly twice the activity of succinylsulfathiazole. In the absence of diarrhea and ulcerated lesions in the bowel a single daily dose of phthalylsulfathiazole will effectively lower the coliform organisms in the feces. The vegetative forms of Clostridia are greatly reduced following the oral administration of phthalylsulfathiazole, and stools are rendered odorless without ordinarily producing a diarrhea. The drug is likewise an effective bacteriostatic agent locally in the bowel, as is indicated by the alteration of the coliform bacteria in the presence of a watery diarrhea. An extensive study of absorption and excretion has shown that an average of 5 per cent of the oral therapeutic dose of phthalylsulfathiazole is excreted in the urine. Analyses of stools reveal that the content of phthalylsulfathiazole and a "free" diazotizable degradation product chemically similar to sulfathiazole varies between wide limits and that this "free" compound may maintain a concentration of 1,250 mg. per hundred grams. The authors describe preliminary trials of phthalylsulfathiazole in nonspecific diarrheas, bacillary dysentery, chronic ulcerative colitis and for the preoperative preparation of the large bowel. The drug appears particularly well tolerated by patients having ulcerative colitis and is quite effective in inducing and maintaining prolonged remissions. Severe toxic manifestations have not been encountered in patients with ulcerative colitis even though the therapy has continued for several months. Phthalylsulfathiazole can be maintained in high concentration in the diseased alimentary tract with low concentrations in the blood. It is suggested that the action of succinylsulfathiazole and phthalylsulfathiazole may not be due either wholly or in part to the formation of sulfathiazole by simple hydrolysis. As indicated by the alteration of the coliform flora in the bowel of man, phthalylsulfathiazole in half the dosage is as effective as succinylsulfathiazole.

Journal of the Mount Sinai Hospital, New York

11:63-136 (July-Aug.) 1944

William Henry Welch Lectures: II. Restoration and Pathologic Reactions of Liver. F. C. Mann.—p. 65.
Newer Advances in Knowledge of Gastritis. B. B. Crohn.—p. 75.
Essays on Biology of Disease. E. Moschcowitz.—p. 83.
Massive Pulmonary Embolism: II. Based in Part on Study of 88 Fatal Cases. H. Neuhof and S. H. Klein.—p. 87.
Life's Later Years: Studies in Medical History of Old Age. F. D. Zeman.—p. 97.
Intracranial Meningiomas. A. T. Kazan, D. Weller and J. Gomez Jaramillo.—p. 105.

Journal of Oral Surgery, Chicago

2:193-288 (July) 1944

Development of Treatment of Jaw Fractures. L. L. Schwartz.—p. 193.
Soft Tissue Surgery. B. E. Luck.—p. 222.
Cleft Palate. J. W. Kemper.—p. 227.
Osteotomy for Correction of Mandibular Malrelation of Developmental Origin. R. O. Dingman.—p. 239.
Plastic Operation for Lengthening Congenitally Short Upper Lip: Preliminary Report. J. F. Ford.—p. 260.
*Monocytic Leukemia with Oral Manifestations: Report of Case. L. F. Aseltine.—p. 266.
Maxillary Cyst: Report of Case. F. W. Coggan.—p. 268.
Ludwig's Angina and Anesthetic Complications. V. H. Frank.—p. 271.
Ameloblastoma: Report of Case. N. H. McDonald.—p. 275.
Multiple Cementoma. J. L. Bradley.—p. 278.

Monocytic Leukemia with Oral Manifestations.—A man aged 66, who was hospitalized with the complaint of "sore mouth," had been treated by his dentist and physician for Vincent's infection since the onset of the oral symptoms, eight weeks previously, but there had been no improvement. Over the gingival tissues and in the mucobuccal fold were several large ulcers that were extremely tender to palpation. Their periphery was irregular, with marginal inflammation. Examination of the neck revealed a lymphadenopathy of the submaxillary and superficial cervical glands. There was also bilateral inguinal lymph adenopathy. The liver and spleen were enlarged a full hand's breadth below the costal margin. Over the trunk and extending onto the legs were painless areas of elevation and induration surrounded by hemorrhage. The blood picture showed a red blood cell count of 2,100,000 and hemoglobin of 51 per cent. The white blood cell count was 102,000 with the cells predominantly immature monocytes. The diagnosis was (1) acute monocytic leukemia, (2) leukemia cutis, (3) secondary anemia, (4) ulcerative leukemic stomatitis. The patient died a few days later. Aseltine stresses that progressive weight loss, persistent oral ulceration, malaise, pallor and skin lesions, any one or a combination of these, should arouse suspicion of a blood dyscrasia. Patients with blood dyscrasias exhibit decreased or little resistance against infection following the removal of teeth, and local necrosis results. The leukocytes are immature and unable to combat infective organisms, and so surgical intervention is definitely contraindicated.

Journal of Pediatrics, St. Louis

25:1-104 (July) 1944

Tibial Bone Marrow Infusions in Infancy. H. I. Arbeiter and J. Greengard.—p. 1.
Bone Marrow Infusions as Routine Procedure in Children. F. Meola.—p. 13.
Treatment of Poliomyelitis. W. B. Snow.—p. 17.
Dust Bronchitis. J. A. Toomey and C. L. Petersilge.—p. 25.
*Pneumonia, Pneumothorax and Emphysema Following Ingestion of Kerosene. E. P. Scott.—p. 31.
Treatment of Meningococcic Meningitis and Septicemia: Sulfadiazine, Sulfanilamide and Serum Therapy. C. W. Cory, C. E. Abbott Jr. and E. G. Truszkowski.—p. 35.
*Treatment of Pertussis with Lyophile Hyperimmune Human Pertussis Serum. I. E. Scheinblum and J. G. M. Bullowa.—p. 49.
Significance of Single and Multiple Shigella Infections in Institutionalized Children. O. Felsenfeld and Viola Mae Young.—p. 56.
Spontaneous Subarachnoid Hemorrhage in Infants and Its Relation to Hydrocephalus. S. G. Babson.—p. 68.
Analysis of Children's Eating Habits. A. L. Baldwin.—p. 74.
Psychologic Care of Children with Pulmonary Tuberculosis. E. L. Kendig Jr.—p. 79.

Pneumonia, Pneumothorax and Emphysema Following Ingestion of Kerosene.—Scott reports the clinical history of a boy aged 2 who was admitted to the hospital two hours after he had ingested from 1 to 2 ounces of kerosene. Before bringing him to the hospital his parents gave him some cream, which caused him to vomit. Because of his apparent pulmonary edema he was given an immediate continuous infusion of 500 cc. of 20 per cent glucose followed by 10 per cent glucose in distilled water. In addition he was given oxygen continuously and caffeine with sodium benzoate. A saline enema followed by a rectal tube was used to relieve the abdominal distention. No gastric lavage was performed. Within two hours the child was conscious. The next morning his temperature had risen to 103.2 F., but he was alert and a bland diet was taken well. In view of the rise in temperature with an elevated white blood cell count, it was thought advisable to administer sulfathiazole.

His temperature became normal three days after admission and remained so until discharge. The roentgenograms revealed aspiration pneumonia, bilateral pneumothorax with possible bronchopleural fistula on the right, and soft tissue emphysema. Treatment was symptomatic except for the sulfathiazole medication. On the seventh day a roentgenogram revealed that the left pneumothorax was clearing. Both lungs had become more homogeneous. The heart was almost in the midline and the soft tissue emphysema was less severe. The patient made an excellent convalescence. Pulmonary manifestations following the accidental ingestion of kerosene are common in young children, but this is probably the first case reported with complications such as pneumonia, pneumothorax and emphysema.

Lyophile Human Serum in Pertussis.—Scheinblum and Bullowa report observations on 23 patients who were selected for treatment because they were considered critically ill with pertussis as judged by their age, the severity of the attacks of paroxysms, apnea, cyanosis and emesis and the presence of pneumonic complications. The dried serum, the equivalent of 20 cc. of whole hyperimmune pertussis serum, was dissolved in 10 cc. of sterile distilled water and thus was concentrated by 50 per cent. Serum was administered intramuscularly to 22 patients; 17 of these patients received three 20 cc. doses, 4 received four 20 cc. doses and 1 received a single 20 cc. dose. Another patient received one 40 cc. dose intravenously, as suggested by McGuinness and his associates. The response of the young infants was apparently better than that of the older children. This may have been due to the fact that the age and weight of the patient were not considered in the dosage given. Sixteen of the 23 patients treated were under 1 year of age. None of these infants died. The 2 children who died were in the 1 to 2 year age group and were moribund when treatment was begun. Treatment early in the course of pertussis was effective. Two patients treated in the eighth and ninth weeks of illness had a good response. There were demonstrable circulating agglutinins following the administration of the serum. Lymphocytosis was suppressed after the administration of the serum. Eleven patients who had pneumonic involvement were treated with the serum in addition to sulfadiazine. There was no extension or recurrence of the pulmonary involvement and no development of pneumonia after a full course of serum therapy.

Journal of Thoracic Surgery, St. Louis

13:271-356 (Aug.) 1944

Current Observations on War Wounds of Chest. B. N. Carter and M. E. DeBakey.—p. 271.
War Wounds of Chest: Observed at Thoracic Surgery Center, Walter Reed General Hospital. B. Blades and D. J. Dugan.—p. 294.
Trends and Practices in Thoracic Surgery in Mediterranean Theater. E. D. Churchill.—p. 307.
*Thymectomy in Treatment of Myasthenia Gravis: Report of 20 Cases. A. Blalock.—p. 316.
Intrapleural Infection with Clostridium Welchi. J. K. Poppe.—p. 340.
*Agenesis of Lung. A. R. Valle and E. A. Graham.—p. 345.

Thymectomy in Myasthenia Gravis.—Blalock reports the results obtained in 20 patients with myasthenia gravis on whom total thymectomy was performed. The duration of illness varied from seven months to twelve years. Four of the patients had had partial remissions. The preoperative neostigmine requirements ranged from 75 to 910 mg. daily. Only 2 of the patients had a thymic tumor. Most of the others presented a persistent two lobed thymus which on microscopic examination showed lymphoid hyperplasia with germinal center formation. Four of the patients have died since operation, three of the deaths occurring in the early postoperative period. Of the 16 remaining patients 3 are well, 5 are considerably improved, 5 are moderately improved and 3 have shown little if any improvement. The early and sustained improvement which has been shown by some of the patients makes it difficult to escape the conclusion that thymectomy was at least partly instrumental in causing the alteration. Unfortunately there is no known method by which one may predict the degree of improvement which may be expected to follow the operation. The results in these cases suggest that the best chances of recovery are to be expected with patients who have not had the disease for an extended period. The 4 patients who no longer require neostigmine had had myasthenia gravis for a year or less.

Agenesis of the Lung.—Valle and Graham present the histories of 2 living patients with agenesis of the lung. One case, that of a white woman aged 41, was proved by an exploratory thoracotomy after a clinical diagnosis was made of massive atelectasis of the left lung due to complete block of the left main bronchus. The other case, that of a white boy aged 5 years, is presumed to be agenesis of the lung since the physical examination showed asymmetry of the chest, absence of breath sounds and flatness to percussion on the left side. Also the x-ray film showed complete opacity on the left with displacement of the trachea toward that side, and the bronchogram showed a complete block of the left main bronchus. A bronchoscopy was performed which confirmed these findings. Review of cases from the literature indicates that absence of a lung is not incompatible with life nor does it preclude a long life. This fact is not surprising in view of what is well known now about the postoperative course of a patient after pneumonectomy. Of the 39 cases collected from the literature 25 were of children under 12 years of age. Eleven patients lived to be more than 19 years of age and 3 were 58, 65 and 72 years, respectively. Both of the authors' patients are living and are in fairly good health at the time of this communication.

Kansas Medical Society Journal, Topeka

45:233-268 (July) 1944

Pulmonary Suppurative Disease: Surgical Management. O. T. Clagett.—p. 233.
Continuous Spinal Anesthesia. G. Owens.—p. 240.
Medicolegal Aspects of Traumatic Neuroses. F. A. Carmichael.—p. 242.

45:269-304 (Aug.) 1944

Thinking Ahead in Public Health. C. C. Applewhite.—p. 269.
Meningococcic Meningitis and Waterhouse-Friderichsen Syndrome. H. W. Day.—p. 273.
Ureteral Calculus—Viscerourologic Complexes. O. W. Davidson.—p. 275.

Kentucky Medical Journal, Bowling Green

42:191-214 (July) 1944

Miliary Lesions in Lung. O. O. Miller.—p. 193.
Neurovascular Lesions of Extremities. A. W. Allen.—p. 195.
Pregnancy with Acute Poliomyelitis: Case Report. Alice L. Wakefield.—p. 199.
Eighteen Months Experience on Induction Board. J. J. Moran.—p. 200.
Preliminary Report of Committee for Study of Infant Mortality in Louisville. Margaret A. Limper.—p. 205.
Undulant Fever. H. S. Frazier.—p. 209.

Maine Medical Association Journal, Portland

35:135-152 (July) 1944

Presidential Address. O. F. Larson.—p. 135.
Infectious Venereal Diseases. P. R. Briggs.—p. 137.
Some Remarks About Aschheim-Zondek Pregnancy Tests: From Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine. Elizabeth Fekete.—p. 139.

35:153-172 (Aug.) 1944

Medical Metamorphosis. A. P. Leighton.—p. 153.
*Browntail Moth: Its Life Cycle. Types of Skin Lesions Produced by Poison Hairs. Report of Case of Recurrent Generalized Urticaria Resulting from Contact with Poison Hairs and Its Subsequent Desensitization. C. W. Steele and W. H. Sawyer Jr.—p. 157.

Recurrent Urticaria Resulting from Contact with Browntail Moth.—According to Steele and Sawyer the browntail moth (Nygmia phaeorrhea) reappeared in great numbers in central Maine during the summers of 1940, 1941 and 1942 with a corresponding increase in the number of cases of dermatitis traceable to contact with it. The caterpillars of this insect feed chiefly on foliage of the apple and related species but may also be found on oak, willow and other common hardwood trees and shrubs. The caterpillars cause both serious poisoning to many human beings and severe economic losses through defoliation of orchards, shade trees and woodlots. In the case reported an unusually high degree of skin sensitivity was shown to the poisonous products of the browntail moth larvae. Poisonous material from the browntail moth caterpillars, from the adult moth or from the nests, when it came in contact with the man's skin produced an immediate severe generalized urticarial response. A test dose of an extract of poisonous material produced a skin reaction. Injections were given at five day intervals through the various dilutions until the maximal dose of the most concentrated solution had been given. Soon after

injections were begun the patient reported that the urticaria was decreasing. He continued to break out locally when exposed, but a generalized eruption did not appear. Two months after completion of the desensitization treatment he reported that he had obtained good symptomatic relief and that the urticaria had practically disappeared. The authors believe that even better results might be obtained if it was possible to make up the desensitization extract from the full grown larvae or from barbed hairs obtained from such caterpillars.

Tennessee State Medical Assn. Journal, Nashville

37:215-254 (July) 1944

Demonstration of Gonococcus Cultures. H. Spitz.—p. 215.
Management of Gonorrhea in General Practice. J. L. Morgan.—p. 216.
Present Status of Rapid Treatment of Syphilis. R. H. Kampmeier. —p. 219.
Management of Some Common Phases of Late Syphilis in Practice. R. H. Kampmeier.—p. 222.
Practical Aspects of Management of Lymphogranuloma Venereum. C. H. Mann.—p. 224.

37:255-290 (Aug.) 1944

Wartime Health Education. V. Johnson.—p. 255.
Physiology of Thyroid Gland and Treatment of Exophthalmic Goiter. W. C. Chaney.—p. 261.
DDT Powder for Destruction of Body Lice. A. L. Ahnfeldt.—p. 263.
Standing Orders for Nurses in Industry. Council on Industrial Health, American Medical Association.—p. 266.

United States Naval Med. Bulletin, Washington, D. C.

43:209-408 (Aug.) 1944. **Partial Index**

Prevention of Flash Burns by Protective Glove Film. G. B. Fauley and A. C. Ivy.—p. 209.
Traumatic Rupture of Spleen. G. M. Perisho and M. Steiner.—p. 216.
Polycystic Disease of Kidneys. S. S. Leiter and J. L. Waterman.—p. 223.
Ambulatory Program Following Operation for Unruptured Appendicitis. C. A. Lauer and R. K. Kerr.—p. 232.
Low Back Pain: Subluxations of Apophysial Joints and Fractures of Articular Facets. W. G. Scott.—p. 234.
Tendon Repair. T. C. Cole.—p. 241.
Reception and Treatment of Casualties Aboard an Assault Transport. B. Gillespie and J. C. Owens.—p. 245.
Working Rules in Field: Supplementary Suggestions on Care of Wounded. E. Holman.—p. 253.
Genital Manifestations of Early Filariasis. R. H. Fogel and R. W. Huntington Jr.—p. 263.
Acute Infectious Hepatitis. V. W. Logan.—p. 271.
Posterior Gonococcal Urethritis. D. H. Pattison and R. A. Burhans. —p. 278.
*Treatment of Cerebrospinal Fever with Penicillin: Preliminary Report. D. H. Rosenberg and P. A. Arling.—p. 281.
Toothache in Low Pressure Chamber. I. W. Brickman.—p. 292.
Endotracheal Anesthesia for Dental and Oral Surgery. W. B. Johnson Jr. and E. R. Ruzicka—p. 304.
"Trench Mouth" Aboard a United States Naval Auxiliary Vessel. D. S. Janetos.—p. 308.
Analysis of Psychiatric Patients Transferred to United States from an Overseas Base. J. N. Williams.—p. 311.
Psychometric Procedure for Screening Mental Defectives. H. M. Hildreth, J. A. Wheeler Jr. and S. B. Williams.—p. 316.
Study of Albuminuria in Applicants for Naval Enlistment. W. A. Murphy.—p. 321.
Occupational Therapy in Naval Hospital. H. V. Hughens and L. O. Parker.—p. 325.

Treatment of Cerebrospinal Fever with Penicillin.—Of the 31 cases of cerebrospinal fever constituting the basis of this report by Rosenberg and Arling, 22 were proved to be meningococcic in origin. In the remaining 9 patients the clinical picture and findings in the spinal fluid were characteristic of meningococcic meningitis, but the stained smears as well as cultures of the spinal fluid and blood did not reveal organisms. Whereas the majority of patients in this series recovered following only one or two intrathecal injections of penicillin (10,000 to 20,000 Oxford units), in the more severe forms of meningitis larger amounts were necessary. As little as 20,000 Oxford units given intravenously over a four hour period, together with one intrathecal injection of 10,000 Oxford units, resulted in recovery in 2 instances. The amount of penicillin required by different patients will vary with the number, type and virulence of the organisms as well as with the immunologic reaction of the host and will be indicated by the clinical and bacteriologic responses. As the clinical picture presented by the patients with bacteremia was indistinguishable from that observed in many patients with negative blood cultures, it is contended that penicillin should be administered both parenterally (intravenously or intramuscularly) and intrathecally to all patients with cerebrospinal fever. It is of paramount importance to continue penicillin intrathecally until recovery is assured. Penicillin need be administered parenterally only during the first twenty-four to forty-eight hours of treatment or for shorter periods in the milder forms of infection.

Virginia Medical Monthly, Richmond

71:395-444 (Aug.) 1944

Rickettsial Diseases in Virginia. H. H. Henderson and Katharine Atwood Walke.—p. 397.
Agranulocytic Angina—A Drug Hazard. E. L. Copley.—p. 416.
*One Day Treatment of Sulfonamide Resistant Acute Gonorrhea with Penicillin: Preliminary Report. S. G. Page Jr. and L. L. Heimoff. —p. 423.
Treatment of Sulfonamide Resistant Gonorrhea with Report of 11 Cases Cured. G. C. Tyler.—p. 425.
Ectopic Pregnancy. H. H. Ware Jr., W. C. Winn, and E. C. Schelin. —p. 428.
Diagnosis and Treatment of Primary Atypical Pneumonia. V. D. Offutt.—p. 431.
Health and Government. F. L. Apperly.—p. 433.

One Day Treatment of Sulfonamide Resistant Acute Gonorrhea with Penicillin.—Page and Heimoff report that 30 cases of sulfonamide fast acute gonorrhea became bacteriologically negative within twelve hours after treatment with penicillin was instituted. Two of the patients had had three courses of sulfathiazole, 11 two courses of sulfathiazole, while 17 had had one course. One hundred thousand units of penicillin was given in five divided intramuscular doses of 20,000 units each, at three hourly intervals, as a complete course of therapy. No toxic effects were noted; blood counts and urinalysis done at three, twelve, twenty-four and forty-eight hour intervals were normal; urethral smears and cultures taken at three hour intervals during the course of treatment became negative within a period of twelve hours.

West Virginia Medical Journal, Charleston

40:245-276 (Aug.) 1944

Traumatic Injuries of Kidneys. G. C. Prather.—p. 245.
Sporadic Meningococcus Meningitis: Report of 2 Cases. W. P. Boger. —p. 248.
Emergency Maternity and Infant Care Program. A. J. Lesser.—p. 254.
Distribution of Pain in Lesions of Upper Urinary Tract: Report of Cases. T. B. Washington.—p. 257.

40:277-308 (Sept.) 1944

*Some of the Uses of Cutis (Derma) Graft Transplant in General Surgery, Orthopedic Surgery and Gynecology. J. E. Cannaday.—p. 277.
Accidents of Pregnancy. S. A. Cosgrove.—p. 283.
Some Dangers of Venesection in Cardiovascular Disease. R. A. Houston. —p. 292.

Uses of Cutis (Derma) Graft Transplant.—The term "cutis graft" means skin from which a thin layer of epidermis has been removed with a skin graft razor. Cannaday suggests that the reason this material is not utilized more widely in this country is the misconception that it is likely to cause epidermoid cysts. There is no record of the development of epidermoid cyst following the use of cutis graft. The cutis graft is gradually infiltrated with and is replaced by connective tissue, so that finally the graft takes on the characteristics of the structure that it replaces. In a hernial repair it is converted into fibrous tissue that resembles aponeurotic tissue, and when used to replace tendon it is rapidly converted into tissue resembling tendon. When used in the reconstruction of joints like the hip and knee joints it takes on the characteristics of normal joint lining. Cutis graft tissue can be used anywhere that fascia lata or other aponeurotic tissue has been used in the past. The author and his associates in the Charleston General Hospital have made use of cutis grafts in a total of 72 cases. The list includes several types of hernia, operations to suspend the uterine cervix for the relief of prolapse, wobbling knees, fractures of the patella, replacement of torn dura, support of the bowel in sigmoid colostomy and the like. Cutis may be used in all cases in which the use of fascia or tendon might be indicated with the expectation of better results. It heals rapidly and well, has great vitality, is able to survive under adverse conditions, possesses great tensile strength, has a good blood supply, gradually assumes the function of the part it replaces and is readily available. Its greatest value, perhaps, is in the repair of large incisional hernias.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Archives of Disease in Childhood, London

19:43-98 (June) 1944

Incidence of Rickets in Wartime. British Paediatric Association.—p. 43.
Survey of Rickets in Lincolnshire (Parts of Kesteven). R. W. B. Ellis and Audrey E. Ellis.—p. 45.
Statistical Analysis. P. Stocks.—p. 48.
*Incidence of Rickets in Children Attending Hospitals in Bristol from September 1938 to May 1941. B. D. Corner.—p. 68.
*Observations on Tuberculous Meningitis. J. McMurray.—p. 87.
Analysis of Fate of Premature Babies in Warwickshire for 1942 and 1943. C. F. Brockington.—p. 93.

Incidence of Rickets in Children Attending Hospitals in Bristol.—Corner describes investigations on the prevalence of rickets among infants under the age of 2 years who were attending hospitals in Bristol during the period from September 1938 to May 1941. Particular emphasis has been laid on the diagnosis of mild rickets during the first six months of the infant's life, as at that stage prophylactic measures would be most useful. Since the clinical diagnosis of rickets is apt to be uncertain in mild cases, the plasma phosphatase was estimated and correlated with the clinical evidence. X-rays were used in only a few cases, and serum phosphorus and calcium estimations were available in some cases. Microscopic examination of the ribs post mortem was carried out in a few cases. Evidence of rickets was searched for in 820 children in the age range of 2 weeks to 2 years. Rickets in which there were clinical signs and either x-ray evidence or an increase in the plasma phosphatase above 15 units was found in 31.4 per cent of the children. A further 3.9 per cent of patients may be considered to be early cases, since they showed no clinical evidence of rickets but the phosphatase was raised above 15 units. Some clinical signs suggestive of rickets were shown by 14.5 per cent of children, but other investigations were negative. There is a correlation between an increase in the plasma phosphatase and definite enlargement of the costochondral junctions, but when the enlargement is only slight the phosphatase is below 15 units in 81 per cent of cases, so that slight enlargement of costochondral junctions alone is not diagnostic of rickets. The incidence of rickets was greatest during the period six to nine months, when it was 52 per cent, and from twelve to eighteen months, when it was 48 per cent. Below the age of 6 months there were 26.2 per cent of definite cases. The incidence of rickets is 5 per cent lower in breast fed infants than in artificially fed infants. There is little difference in the incidence of rickets in infants who were fed on dried milks, milk mixture or sweetened condensed milk. The incidence of rickets in children who had received vitamin D supplement, which, however, often contained less than 400 units in the daily dose, was 10 per cent higher than in the other cases. The incidence of rickets did not show a definite relationship to rate of gain in weight except in the youngest group of infants. The incidence of rickets in twin and premature infants is not greater than the average for the whole age range, but in the youngest group of patients the incidence is doubled in the twin and premature infants. There appeared to be a definite relationship between the incidence of rickets and the type of antepartum diet of the mother. The incidence of rickets was greatest when the mother's diet was poor. Accessibility of direct sunlight and economic status of the family play a considerable part in the incidence of rickets.

Tuberculous Meningitis.—McMurray investigated two aspects of tuberculous meningitis: (1) the question why it does not arise in every case of tuberculous bacillemia and (2) with what frequency the bovine type of tubercle bacillus occurs in tuberculous meningitis. Eleven patients with tuberculous meningitis were examined to determine the pathogenesis of the condition. It appeared that tuberculous meningitis commonly arises as the result of the extension into the subarachnoid space of a focus in the meninges or in the juxtameningeal tissues. This focus is blood borne and may or may not be one of the foci of miliary tuberculosis. Cerebrospinal fluids from 26 cases of tuberculous meningitis have been examined. Tubercle bacilli were found microscopically in 20 and strains have been isolated in 24. Of the 24 strains isolated, 7 were of the bovine type and the other 17 of the human type. All the bovine strains occurred in the 20 children under 15 years of age. The source of infection with the bovine strains could not be established.

British Journal of Dermatology and Syphilis, London

56:107-150 (May-June) 1944

Reticuloses. W. N. Goldsmith.—p. 107.
Lymphadenoma: Its Etiology and Its Skin Lesions. E. C. Warner.—p. 129.

British Medical Journal, London

2:67-102 (July 15) 1944

Current Progress in Sterilization of Air. S. Mudd.—p. 67.
Intravenous Barbiturates in Treatment of Hysteria. C. Lambert and W. L. Rees.—p. 70.
Two Cases of Gunshot Wound Resulting from Unusually Large Missiles: Recovery. R. Charles.—p. 73.
Modification of Invagination Method of Intestinal Anastomosis. J. B. Hogarth.—p. 75.
Method of Locating Mobile Renal Calculus at Operation. B. W. Goldstone.—p. 77.

2:103-136 (July 22) 1944

Some Problems in Riboflavin and Allied Deficiencies. H. S. Stannus.—p. 103.
Two Years of Military Psychiatry in Middle East. H. B. Craigie.—p. 105.
Diagnosis and Treatment of Lesions Due to Vesicants. W. E. Chiesman.—p. 109.
Rupture in a Supposed Lower Segment Cesarean Section Scar. D. W. James.—p. 112.
Meigs's Syndrome: Hydrothorax and Ascites in Association with Fibroma of Ovary. A. C. Clay, R. N. Johnston and L. Samson.—p. 113.

Lancet, London

2:97-130 (July 22) 1944

Naval Experience in Relation to National Health Service. S. Dudley.—p. 97.
*Dissection Lobectomy for Bronchiectasis: Review of 100 Cases. T. H. Sellors, V. C. Thompson and G. Qvist.—p. 101.
*Influenza A Outbreak of October-December 1943. C. H. Andrewes and R. E. Glover.—p. 104.
Vocational Aspects of Neurosis in Soldiers. A. Lewis and K. Goodyear.—p. 105.
Finger Exerciser for Burned Hands. M. C. Oldfield and C. J. King.—p. 109.
Hydronephrosis as Cause of Backache. P. C. Mallam.—p. 110.
Successful Suture of Finger Flexor Tendon. R. M. Jones.—p. 111.

Dissection Lobectomy for Bronchiectasis.—Sellors and his collaborators point out that the dissection method of lobectomy has the advantages over the tourniquet method that the possibility of secondary hemorrhage is much diminished by individual ligation of artery and veins, the chances of fistula formation are diminished by careful closure of the bronchus, sepsis in the hilar stump is eliminated and the removal of the lobe can be said to be total rather than subtotal, which is the case in the tourniquet operation. A further problem in the evolution of the operation is the closure of the bronchus. When a reliable method of bronchial exclusion and the avoidance of fistula is discovered, lobectomy will have reached all the standards required of clean aseptic surgical technic. The 100 cases reviewed here were a consecutive series in which dissection lobectomy was done for suppurative bronchiectasis. The operative mortality was 6 per cent, and good results were obtained in 83 per cent. The most striking feature of the postoperative course has been the low incidence of pulmonary sepsis, and this is probably due to elimination of the hilar slough inevitable with tourniquet lobectomy. The incidence of postoperative atelectasis was high (29 per cent) but secondary pyogenic infection was exceptional. Pleural adhesions tend to lower the incidence of massive collapse, but their most important function is to expedite resolution of this condition. The commonest postoperative infection was tuberculosis, which developed in 7 cases, being fatal in 3. Pulmonary lobectomy by dissection is unquestionably a great advance on the tourniquet operation.

Influenza A Outbreak of October-December 1943.—According to Andrewes and Glover there occurred during the last quarter of 1943 in Britain the most widespread outbreak of influenza since the early months of 1937. Clinically the epidemic was mild. The small amount of influenza prevalent in the early months of 1943 was largely due to influenza virus B, but in April and in most of the summer months localized outbreaks occurred chiefly in service units, and serologic tests

(Hirst's technic) indicated that virus A was concerned. Hirst tests on serums obtained from patients who had respiratory infections between October and December yielded a high percentage of A positives. No rises in titer against influenza B virus was found. The strains isolated readily infected ferrets but were not easily adapted to mice. The serologic evidence indicates that at least 72 per cent—and perhaps 90 per cent—of the cases of influenza studied from October to December 1943 were due to influenza A virus. If the material available was a fair sample of that to be found in the country generally, this was a fairly pure A outbreak. Influenza virus B played no apparent part. Influenza of a similar type prevailed in the United States in the autumn of 1943 and also was predominantly of type A.

Medical Journal of Australia, Sydney

1:477-500 (May 27) 1944

Rh Factor: Laboratory Aspects. Rachel Jakobowicz and Lucy M. Bryce.—p. 477.
*Importance of Rh Factor in Obstetrics. Vera Krieger.—p. 480.
Rh Factor: Ethnological Aspects. R. T. Simmons and others.—p. 483.
Time Saving Mastoidectomy Dressing. J. R. Hutcheon.—p. 485.

1:549-572 (June 17) 1944

Experimental Empiricism in Chemotherapeutic Research. E. Singer.—p. 549.
Rh Factor in Blood of Australian Aborigines. R. T. Simmons, J. J. Graydon and Patricia Hamilton.—p. 553.
Some Reflections on Amnesia, Psychiatric and Forensic. G. L. Ewan.—p. 554.
Medical Applications of Maze Test. S. D. Porteus.—p. 558.

1:573-596 (June 24) 1944. **Partial Index**

Scope of Mental Testing. D. W. McElwain.—p. 573.
Contribution of Mental Tests to Medicine. J. V. Ashburner.—p. 575.
Asphyxia in Newborn. W. K. McIntyre.—p. 580.
Solar Radiation and Pernicious Anemia in South Australia. J. B. Thiersch.—p. 583.

Rh Factor in Obstetrics.—Krieger reviews work on the Rh factor carried out at the Women's Hospital in Melbourne. Rh negative blood tests were made on the blood of all pregnant patients whose previous history had shown evidence of miscarriage or stillbirth. Four hundred and eighty-six such patients were tested between May and October 1943, and 101 (21 per cent) were found to have Rh negative blood. The author reviews the results of tests for Rh antibodies during and after delivery on mothers with Rh negative blood. With regard to the frequency of erythroblastotic children from mating of persons with Rh positive and Rh negative blood, the author finds that not all the babies of a mother with Rh negative blood and a father with Rh positive blood have Rh positive blood. Since the Rh factor is transmitted as a mendelian dominant, the fate of the children depends on the father's being homozygous or heterozygous for the factor. Furthermore, not every mother with Rh negative blood will produce isoantibodies to the Rh factor, and the amount of antibodies formed in any one pregnancy varies considerably. The mildest form of erythroblastosis, the hemolytic anemia of the newborn, may not be diagnosed as such unless attention has been directed to the possibility of its presence. Mild forms of erythroblastotic icterus may be classified as a rather severe ordinary icterus neonatorum if no special investigations are made. Although nothing can be done to prevent the action of Rh substance from the baby from producing Rh antibodies in the mother, or the passage of these antibodies through the placenta into the fetal circulation, the testing for the Rh factor and for Rh antibodies is necessary for several reasons, for instance, for proper blood selection, should either mother or child require a transfusion. The Rh factor should be investigated not only in women whose past history suggests the occurrence of erythroblastosis but in all women attending antepartum clinics at maternity hospitals. The question of the production of sufficient suitable typing serum is all important. Many difficulties are experienced in obtaining blood from the patients, even when a high titered serum has been detected. There is the fact that the titer of antibodies usually decreases rapidly. This necessitates the taking of blood from the patient within a week or two after her confinement. The patient or her doctor may object to this. There is also the question of variability of titer and "polyvalence" in serum from these patients.

Monatsschrift für Psychiatrie und Neurologie, Basel

108:177-232 (Oct.) 1943

Anatomicoclinical Study of Complex Hyperkinetic Syndromes; Late Post-Traumatic Dementia with Progressive Rigidity and Tremor. G. de Morsier and L. V. Bogaert.—p. 177.
*Nonconvulsive Electric Treatment in Depression. P. Plattner and H. Löhnis.—p. 209.
Juxtamedullary Dermoid Cyst. L. Bakay, L. Benedek and A. Juba.—p. 222.

Nonconvulsive Electric Treatment in Depression.—According to Plattner and Löhnis it has been generally accepted that convulsions in the form of epileptic attacks are indispensable for the success of electric and other shock treatments and therefore the aim has always been to avoid incomplete attacks. The unpleasant complications such as wrenching of muscles and fractures were accepted as inevitable or attempts were made to minimize them by posture. Others, particularly American investigators, studied the possibility of reducing the convulsions by the use of curare or magnesium sulfate. The authors also unsuccessfully tried the use of magnesium sulfate but then decided to try weaker currents to avoid convulsions completely. They produced "absences" (temporary suppression of mental function) by passing a current of 60 volts for 0.1 second. The patient loses consciousness for only a few seconds and often is unaware that treatment has been given. More than 50 patients who on the average passed through 20 absences never experienced unpleasant sensations. A number of illustrative cases are reported. The authors conclude that for combating the depressive syndrome by electric irritation of the brain the elicitation of motor manifestations is superfluous and that the essential factor is that other, probably sympathetic, centers are stimulated. The convulsive manifestations may be undesirable secondary effects. It was found that arteriosclerotic and senile depressions can be effectively treated by the use of weaker currents that are tolerated even by old and fragile patients. Stronger currents are necessary in climacteric, involutional and endogenous depressions and such currents may produce convulsions and epileptic attacks, but to avoid the risk of fractures phenobarbital can be given, which does not interfere with the therapeutic effect of the electric current.

Rev. Argent.-Norteam. de Cienc. Méd., Buenos Aires

1:831-926 (Feb.) 1944. **Partial Index**

*Three Tests for Differential Diagnosis of Jaundice. Lola Moyano López.—p. 855.
Traumatic Rupture of Spleen. H. F. Day.—p. 885.

Three Tests for Differential Diagnosis of Jaundice.—Moyano López performed tests of total blood bilirubinemia, phosphatemia and the Hanger test on 321 patients with jaundice. She concludes that the blood bilirubin test is of greatest value in recognizing parenchymal involvement of the liver. The blood phosphatase test is sensitive and reliable in the diagnosis of bile tract obstruction. Hanger's test is of moderate value in the diagnosis of alterations of the liver parenchyma. The average normal value of blood phosphatase in adults varies from 1.5 to 4 Bodansky units. Lower figures indicate a bad prognosis. Blood phosphatase is slightly increased in the course of hepatitis. It may reach an average value of 10 Bodansky units. A lowering of blood phosphatases approaching normal values in the course of hepatitis together with a lowering of the figures of blood bilirubin and a decrease of the Hanger test indicates a favorable course of the disease. A sudden acute increase of blood bilirubin to very high values after a drop to 50 or 90 mg. of bilirubin per thousand cubic centimeters of blood together with unchanged results of the blood phosphatases and Hanger's tests indicate a fatal prognosis. If blood bilirubin reaches high figures and then drops to 80 or 90 mg. and remains at these levels while the blood phosphatase increases beyond 10 Bodansky units and the Hanger test increases, the case is one of hepatitis complicated by bile tract obstruction. In a case of jaundice, if blood phosphatase is slightly above 10 Bodansky units, blood bilirubin about 200 to 300 mg. per thousand cubic centimeters and Hanger's test is faintly positive, jaundice is due to an old obstruction which has affected the liver in such a way as to lead to hepatitis

Book Notices

The Pathogenesis of Tuberculosis. By Arnold R. Rich, M.D., Associate Professor of Pathology, The Johns Hopkins University School of Medicine, Baltimore. Cloth. Price, $10.50. Pp. 1,008, with 90 illustrations. Springfield, Illinois & Baltimore: Charles C Thomas, 1944.

This timely book by Rich, well qualified by training and experience to present the subject of pathogenesis of tuberculosis, is written clearly and in orderly style. It incorporates the basic factors and principles which influence the occurrence of tuberculous infection or determine its progression or arrest. An analysis within the present limits of our knowledge up to 1940, about the time the bibliography ends, considers the influence of each of those factors on the pathogenesis of the disease. This compilation of the literature brings into a unified whole the basic and interdependent but scattered and isolated facts contributed by bacteriology, immunology, pathology, clinical observation, experimental investigation, epidemiology and genetics. The book is broader than previous treatises on tuberculosis alone and includes an analysis of the basic principles that govern infection and resistance in general. Whenever a stand is taken, it is based on the first hand examination of original papers, to which there are 1,417 references, or from the author's personal experiences. In the author's words in the preface, "Those who deal with the manifold problems of tuberculosis in their work or teaching are faced continually with the need of a survey," such as this book presents. The author has endeavored to present the principles of native and acquired resistance and hypersensitivity, as far as they are understood at present, in a manner that will enable those who are not specialists in immunology to understand them readily.

Without becoming too critical, it is hoped that the author will not be content to let this issue stagnate before revamping it at regular intervals for new editions and will seek the advice of others qualified in this field. The shortcomings of single authors for extensive volumes should be recognized. However, full credit should be given Rich for the stupendous task he has performed in preparing a volume on the pathogenesis of tuberculosis the equal of which has never before appeared in English. His subject is driven methodically toward a goal beginning with the relations of the chemical constituents of the bacillus to pathogenesis, in which he displays chemical capability. The types of bacilli, variations in form and potentialities are well defined. Under virulence he points out that the study of the bacilli from human sources is not adequately fulfilled nor can we regard different forms of spontaneous disease as being specifically determined by the degree of virulence of the infecting bacilli. Native resistance is elaborately considered in four complete chapters to the conclusion of its mechanism. Following local tissue resistance, hypersensitivity and its mechanism are dwelt on, leading into the problem of specific and nonspecific desensitization; this chapter will require radical modification in new editions because of the uncertain status of this phase of tuberculosis prior to 1940. The mechanism of acquired resistance is fully detailed and climaxed by a good chapter on the factors that influence resistance. The influence of the number of bacilli impresses one with how a simple phase of tuberculosis still requires elucidation. Finally the problems responsible for the characteristics of tuberculous lesions and symptoms, exogenous or endogenous reinfection and the application of the principles of pathogenesis as illustrated by tuberculosis of the lungs, meninges and serous cavities complete the picture of tuberculosis sufficiently to conclude with the decline in the mortality and the future outlook, which becomes the expression of the author as to the importance of each of the major factors. Rich does not appear to contribute to the view that tuberculosis will be self extinguished with the mortality curve trend. He feels that "the disease that still kills more than twice as many individuals as any other single cause of death during this (15 to 44 years of age) particularly productive and enjoyable period of life span can hardly be jubilantly regarded as being 'nearly conquered.'" To the latter view most tuberculologists and investigators will certainly contribute at present. Such a view also attests the need for this volume, and it is doubtful whether any single author could have done a better job with so complex a problem as the pathogenesis of tuberculosis and all its implications than Rich did.

The volume is well composed and is worth possessing. It will help students and medical men to a better understanding of tuberculosis.

Simplified Diabetic Management. By Joseph T. Beardwood Jr., A.B., M.D., F.A.C.P., Associate Professor of Medicine, Graduate School of Medicine, University of Pennsylvania, Philadelphia, and Herbert T. Kelly, M.D., F.A.C.P., Associate in Medicine, Graduate School of Medicine, University of Pennsylvania. Fourth edition. Cloth. Price, $1.50. Pp. 172, with 9 illustrations. Philadelphia, London & Montreal: J. B. Lippincott Company, 1944.

As a manual for the diabetic patient, this volume covers the ground thoroughly and in a manner both concise and clear. The present edition is somewhat revised, notably by the addition of a section on the newer insulin preparations with prolonged action. The inclusion of crystalline insulin among the latter is a rather surprising lapse in an otherwise accurate presentation. The authors present two systems of diet calculation, the unit method and the percentage method. Both are clearly and simply explained and accompanied by the appropriate tables of food values. However, it is apparent that the authors have abandoned their earlier use of the diet prescription chart based on the "line-ration schemes" of Lawrence and of Christian and O'Hara. In view of this it is rather strange that, although all reference to it has been removed from the text, the chart is still included in the volume and is still featured in the blurb on the dust cover.

Conferências do curso de aperfeiçoamento de psiquiatria de guerra (organizado pelo Prof. A. C. Pacheco e Silva sob os auspícios da Faculdade de medicina da Universidade de S. Paulo e dos fundos universitarios de pesquisas para da defesa nacional). Paper. Price, Cr. $50.00. Pp. 304, with 11 illustrations. São Paulo, 1943.

The volume presents the twenty-two lectures given during 1943 in a postgraduate course on war psychiatry organized by Dr. Pacheco e Silva, professor of psychiatry in the University of São Paulo. Dr. Pacheco e Silva and fifteen of his colleagues have embodied a thorough study of the various applications of psychiatry to the problems of war; considering first the general scheme of examinations, they proceed to the various clinical pictures as met in a military setting, then to such problems as malingering, laws and regulations, and mental hygiene, individual and collective. The volume is substantial evidence of the foresight and progressive scholarship of our psychiatric colleagues in Brazil.

The Woods Hole Marine Biological Laboratory. By Frank R. Lillie. Cloth. Price, $4. Pp. 284, with 28 illustrations. Chicago: University of Chicago Press; London: Cambridge University Press, 1944.

The Woods Hole Marine Biological Laboratory is a unique institution located on the south shore of Cape Cod on a spit of land between Buzzards Bay on the one side and Vineyard Sound on the other. It is a research and collecting institute joined by strong ties to departments of zoology in many of the country's leading universities. Its importance to medicine lies in its fundamental contribution to an allied science and in the not inconsiderable number of physicians who have received early biologic training in this laboratory. Professor Lillie has been closely connected with the laboratory since its earliest days, and it is both fortunate and appropriate that he should be the author of this welcome history of its scientific and economic development.

Leukopenia and Agranulocytosis. By William Dameshek, M.D., Clinical Professor of Medicine, Tufts College Medical School, Boston. Edited by Henry A. Christian, A.M., M.D., LL.D., Clinical Professor of Medicine, Tufts College Medical School. [Reprinted From Oxford Loose-Leaf Medicine with the Same Page Numbers as in That Work.] Cloth. Price, $1.75. Pp. 841-852. New York, London & Toronto: Oxford University Press, 1944.

This monograph summarizes the present knowledge of conditions in which the leukocyte count is decreased. The material is timely, for, as Dr. Christian says in the preface, "interest in leukopenia and agranulocytosis has been increased markedly in the present period because not infrequently both appear as toxic manifestations of the therapeutic use of sulfonamide drugs." The subject matter is well arranged and presented, and the bibliography of 152 references is selected from the rather extensive literature on the subject. Of especial value are the sections on etiologic factors and on treatment.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

MORTALITY OF BREAST AND BOTTLE FED INFANTS

To the Editor:—**Can you give me information on the proportion of women who can nurse their babies? Most physicians now seem to advise bottle feeding as at least equally desirable. What is the comparative mortality of breast and bottle fed babies?**

Mabel D. Murphy, M.D., Glendale, Calif.

ANSWER.—Sanford (Various Complementary Feedings Used During the Neonatal Period, THE JOURNAL, Aug. 5, 1939, p. 470) in a study of 4,622 infants during the newborn period found that 14 per cent of the mothers were unable to nurse their babies, 30 per cent required some complementary feeding and 56 per cent were able to give their babies sufficient breast milk by the end of the tenth day of life. Statistics on the mortality of breast and bottle fed babies are open to criticism unless they represent the same group and environment and are large enough and cover a long enough period of time to make a fair comparison. In the Infant Welfare Society of Chicago from 1924 to 1929 in 20,000 babies under 1 year of age in which 91.5 per cent were completely or partially breast fed and 8.5 per cent artificially fed, the mortality was 11 per thousand. Of this mortality 66 per cent were artificially fed, 27.2 per cent partially breast fed and 6.7 per cent completely breast fed. In the same organization in 1943, 6,702 babies under 1 year of age were cared for with approximately the same proportion of feeding. The mortality has now dropped to 4 per thousand, but still of this mortality 65 per cent were artificially fed, 28 per cent partially breast fed and 7 per cent breast fed.

DIFFERENTIAL DIAGNOSIS OF APICAL OPACITIES

To the Editor:—**A soldier aged 23 was hospitalized four months ago and carefully studied because of the presence of infiltrative lesions of both lung apexes. Diagnosis of atypical pneumonia was finally made. The patient has now been asymptomatic for about three months. He states that he feels well, and his general appearance is that of a person in good health. However there is no x-ray evidence that the lesions are either regressing or progressing. Other data are negative. Would this man be qualified for full duty or light duty or should he be hospitalized until the lung lesions have disappeared?** **Lieutenant, M. C., A. U. S.**

ANSWER.—What led to the discovery and careful study of the abnormal shadows in the lungs? Were they discovered during and after an acute sickness resembling virus pneumonia? If the soldier actually had a form of virus pneumonia the residual changes in the lungs are probably of no importance and he would be qualified for full duty. Residual shadows are common after virus pneumonia because of the interstitial location of the lesions. Nevertheless, it is unusual for changes to persist so long and in both apexes. Under the circumstances mentioned, unless the acute attack was observed, it is not safe to make a diagnosis of virus pneumonia in retrospect simply because of the changes recorded, as apparently was done. The abnormality may have been present for a long time before. The roentgenogram made at the time of induction should be reviewed for comparison.

Pulmonary tuberculosis is a strong possibility as the cause of the apical densities, and the case should probably be regarded as such until proved otherwise. Further appropriate investigation along this line is advised. Virus pneumonia and pulmonary tuberculosis are sometimes difficult to differentiate, as recently discussed by Yaskalka (*Am. Rev. Tuberc.* **49**:408 [May] 1944). The management of a suspected case of tuberculosis is fully covered in Army Medical Regulations.

GAUZE SPONGE IN ABDOMINAL SURGERY

To the Editor:—**Please give an opinion on the use of the small dry gauze sponge in the abdominal cavity. If intestines are held and they slip, will such a sponge cause adhesions?**

J. Louis Waldner, M.D., Loveland, Colo.

ANSWER.—It is not possible to predict whether or not in any given case adhesions will form following an operation. Traumatizing the peritoneum favors formation of adhesions. If the intestine is to be held for any length of time, it would be preferable to use a wet sponge rather than a dry gauze sponge as suggested in the query.

HOMOSEXUALITY AND ENDOCRINE IMBALANCE

To the Editor:—**At one of our clinical conferences we discussed the subject of homosexuality. It was the opinion of one of the medical officers that recent work has shown an excess of estrogen in the blood, spinal fluid and urine in a large number of homosexuals of both overt and latent types. This was disputed by another medical officer, who claims that recent work at Hartford, Baltimore and Philadelphia has failed to show any such findings. In view of the fact that our medical references are inadequate, I take this opportunity to ask the following questions: 1. What is the latest concept concerning the estrogen content in (*a*) homosexuals, overt type, and (*b*) homosexuals, latent type? 2. What is the latest work done on this subject, where was it done, and what are the findings? 3. Is the treatment of homosexuals purely a psychiatric problem, an endocrine problem or both? 4. What percentage of homosexuals do show endocrine imbalance, and what type imbalance is it?**

M.D., Washington.

ANSWER.—Surprisingly little quantitative laboratory work has been reported in the study of homosexuality from an endocrine point of view. The most recent publication is by Abraham Myerson and Rudolph Neustadt (Bisexuality and Male Homosexuality: Their Biologic and Medical Aspects, *Clinics* **1**:932 [Dec.] 1942). This article provides, in addition to discussion, an adequate bibliography of the other recent work. These authors agree fundamentally with the conclusions of C. A. Wright (*M. Record* **154**:60 [July 16] 1941) that the commonest pattern in the urinary excretion of male homosexuals is a relative increase in estrogenic substance and decrease in androgenic substance. This is not always an absolute increase or decrease from the normal pattern. Myerson and Neustadt state that "it becomes necessary, in all candor, to point out certain serious shortcomings in the chemical studies of urine hormonology: (1) Urine is an excretion and, therefore, cannot adequately measure endocrine activity; (2) the methods are imperfect and, for example, do not measure testosterone but only its breakdown products; (3) inert chemical substances, so far as sexual activity is concerned, participate in the color reactions, and so some falsification of the values occurs; (4) the patients do not live under standard experimental conditions. Nevertheless, and despite all these shortcomings, certain clinical facts are correlated to the urinary findings in definite ways, so that diagnostic facts of importance emerge."

It should be noted that the conclusions of Wright and his group have been vigorously challenged by A. C. Kinsey (Homosexuality: Criteria for a Hormonal Explanation of the Homosexual, *J. Clin. Endocrinol.* **1**:424 [May] 1941). The objections raised are on the basis of inadequate grounds for statistical conclusions by the authors. Kinsey produces evidence of a frequent homosexual tendency among males who also have heterosexual interests and capacities but contributes no further information about the hormone picture.

It is manifestly too soon in the process of endocrine study of this field to answer the question about the percentage of homosexuals who show endocrine disturbance, let alone to decide how frequently homosexuality is an endocrine, how frequently a psychiatric, problem. Myerson and Neustadt feel that they see evidences of endocrine disturbance in 83 per cent of all cases of overt male homosexuality examined as compared to a similar endocrine disturbance in not more than 2.5 per cent of other cases studied. They are unable to come to any conclusion as to which is primary, the psychologic or the endocrine disturbance.

PSORIASIS

To the Editor:—**For several years I have had moderate psoriasis; at times it is clear, and again it becomes severe. It is worse at present on the scalp and the arms and legs. Exposure to sunlight, less effectively to ultraviolet radiation, daily, for thirty days practically eliminates the psoriasis. However, it is impossible for me to do that, being so busy. Have large doses of vitamin D, by mouth, given equivalent results to those obtained by daily exposure to sunshine? Would it be advisable to take the oily vitamin since most patients with psoriasis have a high cholesteremia? Would the oil increase the cholesteremia? The studies on lipocaic which were demonstrated at the session of the American Medical Association in Cleveland were encouraging, but I have seen no reports on that since. Is lipocaic available to the general practitioner as yet? What suggestions can be offered for the treatment of this stubborn disease?**

M.D., Iowa.

ANSWER.—Cedar and Zon (Treatment of Psoriasis with Massive Doses of Crystalline Vitamin D and Irradiated Ergosterol, *Pub. Health Rep.* **52**:1580 [Nov. 5] 1937) treated 15 patients with psoriasis, all between 30 and 50 years of age and all with old psoriasis resistant to treatment. They were given pure crystalline vitamin D in sesame oil, 50,000 units to the capsule containing 5 minims (0.3 cc.) of sesame oil, six capsules per day. These were taken between meals to avoid any augmentation of their action by milk products in the diet, as suggested by Lewis (*J. Pediat.* **8**:308 [March] 1936). Of these patients 11 were cleared of lesions in from six to twelve weeks of treatment. The blood calcium was estimated at intervals and was

seen to increase slowly in all but 1 case. It reached 12 mg. per hundred cubic centimeters in some and up to 16 mg. per hundred cubic centimeters in others. Three untoward reactions were seen in the tenth to the twelfth week of treatment: anorexia, nausea and urinary frequency. These reactions occurred after the lesions of the skin had cleared, and they disappeared on cessation of treatment. Patients with calcified pulmonary tuberculosis, as evidenced by roentgen examination, were excluded from this group to avoid possibility of absorption of the protective calcium. Six patients had mild recurrences in from eight weeks to five months after treatment had been stopped. One of these responded to a second and again to a third course of treatment for eight to ten weeks. Four other cases had remained clear of lesions three to eight months after the end of the treatment.

Neither vitamin D nor lipocaic can produce results to equal those of actinotherapy in the treatment of psoriasis. Most dermatologists get better results from the Goeckerman treatment than from any other one method. O'Leary (Goeckerman Method of Treating Psoriasis, *Canad. M. A. J.* **48**:34 [Jan.] 1943) describes it in detail as practiced in the place of its origin. The ointment, consisting of

	Gm. or Cc.
Crude coal tar	2.0 to 4.0
Zinc oxide	2.0
Corn starch	50.0
Petrolatum to make	100.0

is applied thickly and a suit of cheap underwear is worn over it. Once a day the ointment is removed except for a thin film and the ultraviolet light given through this film, enough to cause a slight erythema. The dose is increased daily to maintain the erythema without causing blisters. Then the patient spends one-half to two hours in a bath at 95 F. After this the ointment is again applied. Every other day autohemotherapy is given, the series ending with the fifth treatment. On the scalp, in place of the coal tar ointment, one containing 5 per cent ammoniated mercury and salicylic acid is used. This course of treatment necessitates a stay in the hospital for two weeks. Most dermatologists find the hospital treatment hard to sell to their patients, who prefer a longer course of milder treatment compatible with continued work. Keim's modification calls for application of a 2 to 10 per cent crude coal tar in cetyl alcohol emulsion base before retiring, and in the morning a tar bath. At the doctor's office undiluted solution of coal tar is painted on each lesion before the ultraviolet treatment is given.

HARRIS DRIP PROCTOCLYSIS—"GAS PAINS"

To the Editor:—**What is the present status of the Harris drip used postoperatively? Does it reduce distention? How much water is absorbed by this method in twenty-four hours? Does it produce peristalsis in the small intestine? If it does, is not this harmful in the presence of peritonitis? What are "gas pains?" Can you tell me when the original paper on this method was published?** **Frances B. Doyle, M.D., Brooklyn.**

Answer.—The Harris drip, unlike the continuous drip proctoclysis first introduced by the late Dr. John B. Murphy, has never been adopted extensively by the profession, and many experienced surgeons and clinicians are unfamiliar with it. The available literature on this method is conspicuous by its extreme paucity. In the light of current methods of preoperative preparation and postoperative treatment its present status must be considered as obsolete in large measure. There are no available recorded observations on the influence of the Harris drip on distention, on the amount of water absorbed in a twenty-four hour period or on its influence on peristalsis in the small bowel. The late Joseph Blake of New York, in a discussion of the postoperative treatment of infective peritonitis (Nelson Loose Leaf Surgery **5,** pp. 22-23), regarded the Harris method as superior at that time.

There appear to have been few authoritative experimental or clinical observations with respect to the factors underlying the production of "gas pains." Such gas pains have been attributed to a variety of causes, including preoperative or postoperative purging, the excessive use of opiates, the nature of the anesthetic, rough handling of tissues during operation, too early or too late feedings and the like. A conventional discussion of the subject is found in Cutting's Principles of Preoperative and Postoperative Treatment (New York, Paul B. Hoeber, Inc., 1932, pp. 311-342). However, Mendes-Ferreira's roentgenologic observations on human subjects (*Proc. Staff Meet., Mayo Clin.* **13**:222 [April 6] 1938) greatly discount the importance of gas in the genesis of postoperative abdominal pains, so that the expression "gas pains" is in all probability a misnomer. No reference has been found to any published original paper on the Harris method.

INDUSTRIAL EXPOSURE TO MERCUROUS CHLORIDE

To the Editor:—**A problem has arisen in a drug manufacturing business. The main product is a venereal disease prophylactic. The women who fill the tubes and clip, wipe and pack them naturally get calomel ointment (33⅓ per cent) on their hands, but they are instructed to wash their hands well with soap and warm water, using a brush, at noontime and again before leaving for home in the evening. Until recently no employee has complained of mercurial poisoning. One employee, after six weeks of this work, was confined to bed for ten days, complaining of pains in various joints, especially the knees, ankles and spine; she also had diarrhea but no soreness of the gums. At the time of her illness she had just completed a course of eight injections, twice weekly, of synodal. Another employee about 45 years of age after three weeks' work complained of stiffness and pains in the joints, especially in the legs, but no soreness of the gums or diarrhea. I insisted that these 2 women were not suffering from mercurial poisoning because of the lack of typical symptoms of mercurial poisoning, their careful personal hygiene, the lack of abrasions on the hands, the shortness of time of employment, and the fact that there have been no other cases among many employees since 1921.** **R. M. Nicholson, M.D., Los Angeles.**

Answer.—The manifestations reported do not suggest mercury poisoning. Joint pains and diarrhea are sometimes present in mercury poisoning, but not as the most characteristic features. On the other hand, the absence of stomatitis and gingivitis by no means rules out mercury poisoning, since their absence is frequent. Mercurous chloride is so insoluble that neither mercury dermatitis nor systemic involvement often occurs. Trivial absorption through the skin may take place, but absorption from the lungs after inhalation of mercurous chloride dust has been denied. In pharmaceutical houses many thousands of man-days have been devoted to the manipulation of this substance without the causation of mercury poisoning. One large manufacturer reports that over a period of years not a single instance of either mercury dermatitis or systemic poisoning from mercurous chloride has appeared among the workers handling this substance.

Even after intramuscular injection of calomel, as in the treatment of syphilis, absorption is not certain. Andrews states that "the insoluble salts such as calomel are so slowly and irregularly absorbed that their use is attended by hazards of prolonged ineffectiveness due to failure of absorption or prolonged overdosage due to tardy absorption." Directly in contact with the skin, mercurous chloride infrequently causes skin pigmentation, which may be persistent.

It appears to be true that, when mercury poisoning arises from mercurous chloride, in most instances some fortuitous event has led to the transformation to the mercuric state. A wide variety of chemicals effect this change, but such chemicals are not likely to be on hand under the circumstances of the operations mentioned in this query. On a theoretical basis, long exposure of calomel to sunlight may change the state of calomel to mercury bichloride, as may also long continued elutriation.

In this instance mercury poisoning is regarded as improbable from the information furnished, but various steps might be utilized to eliminate uncertainty. Quantitative determination of mercury should be made on both urine and blood. However, such determinations do not represent simple laboratory tests. The quantity of mercury in the atmosphere, should atmospheric mercury be suspected, may be measured through the use of the General Electric mercury detector. Most important of all, thorough clinical examinations should be carried out, following the procedures indicated in United States Public Health Service Bulletin 263, published in 1941 and entitled "Mercurialism and Its Control in the Felt-Hat Industry."

ESTROGENIC HORMONE THERAPY AND CANCER

To the Editor:—**Has it been proved that overuse of estrogenic substances might induce cancer? I have been using 1.5 cc. five times monthly of the 10,000 international units. Is this correct or "overuse"?** **Louis L. Sherman, M.D., Oakland, Calif.**

Answer.—Estrogenic substances may induce cancer in animals. There are records of cases in man which suggest that tumor formation has followed estrogenic therapy. However, the true dangers have not been definitely outlined; they have merely been suggested, so that all who use estrogenic therapy should do so with caution. Regarding the prescribed dosage, it is difficult to say whether this represents "overuse" without knowing how long it has been continued and under what conditions. New and Nonofficial Remedies suggests a dosage for estrogenic substances of from 2,000 to 20,000 international units injected one or more times weekly, depending on the response of the patient. After relief has been produced, dosage should be lowered to a maintenance level. Dosage varies for other conditions, such as kraurosis vulvae and gonorrheal vaginitis in children.